JAN 16 1945

Registered at the G.P.O., Sydney, for Transmission by Post as a Newspaper. Published Weekly. Price 1s.

Medical Library

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—31ST YEAR. SYDNEY, SATURDAY, DECEMBER 2, 1944. No. 23.

COMMONWEALTH OF AUSTRALIA. DEPARTMENT OF HEALTH.

Important Notice to the Medical Profession

PENICILLIN

"Commonwealth"

IS MORE FREELY AVAILABLE FOR TREATMENT OF THE CIVILIAN POPULATION

The Medical Profession is notified that the Control of Penicillin Order, promulgated in the Commonwealth of Australia Gazette No. 85 of 3rd May, 1944, has been revoked.

The Penicillin Order published in Gazette No. 189 of 20th September, 1944, and in "The Medical Journal of Australia" of 30th September, 1944, relaxes the conditions under which Penicillin may be supplied for the treatment of members of the civilian population.

To obtain Penicillin a Medical Practitioner must apply in the form of certificate set out in the order to the Senior Commonwealth Medical Officer in the State concerned. The signature of a colleague is no longer required.

PENICILLIN "COMMONWEALTH" (THE SODIUM SALT OF PENICILLIN) IS AVAILABLE IN THE FOLLOWING SIZES:

1 ampoule containing 100,000 Oxford units **£1**
This quantity is sufficient for a series of parenteral doses.
(Available also in boxes holding 5 ampoules.)

1 ampoule containing 15,000 Oxford units .. .. **5s. 6d.**
This quantity is intended for a single parenteral dose.
(Available also in boxes holding 6 ampoules.)

1 ampoule containing 5,000 Oxford units .. .. **3s. 6d.**
This quantity is intended primarily for dilution and local application, but may be used for parenteral injection if desired.
(Available also in boxes holding 6 ampoules.)

Limited quantities only of the sizes 15,000 units and 5,000 units are available at present.

The addresses of the Senior Commonwealth Medical Officers are: **NEW SOUTH WALES,** Customs House, Circular Quay, Sydney; **VICTORIA,** A.C.A. Building, 118 Queen Street, Melbourne; **SOUTH AUSTRALIA,** C.M.L. Building, 41-47 King William Street, Adelaide; **WESTERN AUSTRALIA,** 4th Floor, G.P.O., Perth; **TASMANIA,** Commonwealth Health Laboratory, Launceston; **QUEENSLAND,** Anzac Square, Adelaide Street, Brisbane.

COMMONWEALTH SERUM LABORATORIES

PARKVILLE, N.2, VICTORIA, AUSTRALIA

DRESSING GOWNS
of Spun Rayon Silk

The firm weave and long wearing material of these Polka Dot Dressing Gowns ensure the long service that coupon restrictions demand. They have self sash and gauntlet cuffs. Obtainable in Navy Blue and Maroon.

PRICE 80/10
15 coupons

The House of

PEAPES

AT WYNYARD STATION, GEORGE STREET, SYDNEY
Opposite Hunter Street

STUDENTS' AIDS SERIES
Books of Real Assistance to every Student

NEW TITLES—

Aids to Anæsthesia. By Major Victor Goldman, L.R.C.P., M.R.C.S., D.A.
Price 5/-. Pp. viii + 235. 58 Illustrations.
"Best practical little book on the subject in existence."—*Clinical Journal.*

Clinical Pathology. By David Haler, M.B., B.S. (Hons.) Lond., D.C.P. London. 6/-.

NEW EDITIONS—

AIDS TO:			Orthopædic Surgery and Fractures.		
Anatomy (Pocket Anatomy).	10th Ed.	5/6		2nd Ed.	6/-
Biochemistry.	3rd Ed.	5/-	Osteology.	4th Ed.	5/-
Dispensing.	3rd Ed.	4/-	Pathology.	8th Ed.	5/-
Analysis of Food and Drugs.	6th Ed.	10/-	Pharmaceutical Latin.	2nd Ed.	4/-
Forensic Pharmacy.	3rd Ed.	4/6	Physiology.	3rd Ed.	4/6
Materia Medica.	3rd Ed.	5/-	Surgery.	7th Ed.	10/-
Mathematics of Pharmacy.	2nd Ed.	4/-	Surgical Anatomy.	2nd Ed.	4/6
Obstetrics.	11th Ed.	4/-	Tropical Medicine.	4th Ed.	5/-

RECENTLY REPRINTED—

AIDS TO:					
Bacteriology.	5/6	Dermatology.	5/-	Neurology.	5/6
Biology.	4/-	Medical Diagnosis.	5/6	Ophthalmology.	5/-
Botany.	4/-	Embryology.	4/-	Psychiatry.	5/-
Inorganic Chemistry.	5/6	Forensic Medicine.	4/-	Psychology.	4/-
Organic Chemistry.	4/-	Gynæcology.	4/-	Public Health.	5/-
Physical Chemistry.	5/6	Histology.	4/-	Sanitary Science.	5/6
Diseases of Children.	5/-	Medicine.	5/6	Zoology.	5/-

BAILLIÈRE, TINDALL & COX *7-8, Henrietta Street, London, W.C.2*

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—31ST YEAR. SYDNEY, SATURDAY, DECEMBER 2, 1944. No. 23.

Table of Contents.

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES— Page.
The Blood Groups of Australian Aborigines, by Harold Wilson, J. J. Graydon, R. T. Simmons and Lucy M. Bryce .. 581
Recent Advances in the Treatment of Carcinoma of the Prostate, by D. Coleman Trainor, M.B., Ch.M., F.R.C.S.E. .. 589
The Rational Treatment of Burns, by S. A. Sewell, M.B., B.S., M.R.A.C.P. .. 590

REPORTS OF CASES—
A Report on Two Cases of Ruptured Urethra, by Robert S. Lawson, M.S., F.R.C.S., F.R.A.C.S. .. 592

REVIEWS—
Aviation Medicine .. 593
Medical Bacteriology .. 594
After-Treatment .. 594
Histology for Medical Students .. 594

LEADING ARTICLES—
Penicillin in the Treatment of Syphilis .. 595

CURRENT COMMENT—
Treatment by Alkalies in Blackwater Fever .. 596
Antituberculosis Work in Western Australia .. 597

ABSTRACTS FROM MEDICAL LITERATURE— Page.
Ophthalmology .. 598
Oto-Rhino-Laryngology .. 599

BRITISH MEDICAL ASSOCIATION NEWS—
Scientific .. 600

CORRESPONDENCE—
Muscle as a Hæmostatic .. 600
Note on Cutaneous Leishmaniasis in the Territory of Papua .. 601
Traumatic Monocular Glaucoma .. 601
Scrub Typhus .. 601

OBITUARY—
John Fullarton Mackeddie .. 601

NAVAL, MILITARY AND AIR FORCE—
Casualties .. 603

AUSTRALIAN MEDICAL BOARD PROCEEDINGS—
New South Wales .. 604

NOMINATIONS AND ELECTIONS .. 604
BOOKS RECEIVED .. 604
DIARY FOR THE MONTH .. 604
MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 604
EDITORIAL NOTICES .. 604

THE BLOOD GROUPS OF AUSTRALIAN ABORIGINES.

By HAROLD WILSON, J. J. GRAYDON, R. T. SIMMONS AND LUCY M. BRYCE,[1]

From the Commonwealth Serum Laboratories, Melbourne.

THE sparse aboriginal population of Australia has decreased greatly since the arrival of the white man. It is, therefore, a matter of urgency that anthropological studies of this unique people should be accomplished while opportunity yet exists. In this paper are reported the results of an examination of their blood groups.

In this introduction we have drawn upon the works of Dobzhansky (1937), Boyd (1939, 1940), Wiener (1939), Haldane (1940) and Schiff and Boyd (1942). A fully documented discussion of the geological evidence for the antiquity of prehistoric man in Australia and Tasmania is given by Mahony (1943). The Tasmanian aborigines are extinct; much interest is attached therefore to the description by Tindale and Birdsell (1942) of some Tasmanoid tribes in a "refuge area" of jungle in north Queensland. Birdsell and Boyd (1940) also have examined, on some islands in Bass Strait and in New South Wales, the descendants of mixed groups which included seven Tasmanian women.

One of the aims of study of the physical characters of human populations is to classify them in the hope of throwing light upon their ethnology. Many studies have been concerned with such physical characters as, for example, the shape of the head, the stature and conformation of the body and the colour of the skin, hair and eyes, which are almost certainly adaptive—that is, are capable of being influenced by environment or selection. Moreover, although something is known of the factors governing inheritance of hair and eye colour, inheritance of the other characters just mentioned is determined by various unrecognizable genes, so that the genetic constitution of the people under observation cannot be ascertained by a study of them.

Boyd (1940) has postulated five requirements for any method of physically classifying mankind. (i) The method should be objective—that is, the results should not be subject to the opinion of the investigator, and they should be capable of being proved and compared with those of others. (ii) The physical character studied should be little influenced by environment—that is, it must be due to inherited factors which are known to be determined by genes, the variation in which is predictable. (iii) It should be determined by one or by very few genes. (It would, of course, be an advantage to study many genes if we had means of distinguishing them.) (iv) It should not be subject to the influence of selection. (v) Its mutation rate should be low.

Classification according to blood-group frequencies fulfils these postulates. Provided that right technique and controls are used, such classification is quite objective. There is no evidence and it is unlikely that blood groups are influenced by environment or by selection. They are determined by few genes, the frequency of which can be calculated in any population sampled, and their frequencies cannot be explained by mutation rates of any order which it is reasonable to postulate, the present frequencies being derived (Boyd and Haldane) from the time when man was a comparatively rare animal living in small, isolated communities.

After an isolated population has reached genetic equilibrium, the proportions of the blood groups remain approximately constant from generation to generation. It follows that existing blood-group frequencies are inherited from an earlier past than are most other physical characters that have been studied, and that the information afforded by them is referable to remote human origins. Indeed, the blood groups are probably coeval with man, although this proposition is hardly susceptible of proof. All four of the A, B groups have been recognized

[1] In collaboration with field workers.

in the blood of anthropoid apes. Their presence has also been demonstrated in the mummies of persons who lived about 5,000 years ago; albeit this space is but a very small fraction of the span of existence of the human species. Also, the blood groups are inherited according to simple genetic laws, and therefore the results of investigations into their relative frequencies can be examined mathematically and certain technical errors can often be revealed or excluded by the internal evidence thus obtained.

The Hirschfelds (1919) first perceived differences in the frequencies of the A, B groups in the blood of different populations, and it is now recognized that determination of blood-group frequencies, including those of the sub-groups, the M, N factors and the Rh factor, is one of the few means of physically classifying mankind by which the geographical distribution of genes can be mapped. It is not to be expected that the geographical distribution of the genes of the several blood-group systems should correspond to one another or to the geographical variations in other physical characters which are not determined by the same genes; each character should be studied and assessed separately.

The geographical distribution of genes may be influenced by mutation, selection, inbreeding, mixture (migration) or isolation. So far as the blood groups are concerned, the influence of the first two factors may be disregarded.

Intense inbreeding (see Appendix D) for many generations results in the appearance of a high proportion of homozygotes without, however, affecting the frequency of the genes. This effect is abolished by one generation of random mating.

As a result of migration, an exchange of genes in otherwise isolated communities may take place. The gene frequency of a mixed population can be calculated if the gene frequencies of the original groups comprising the mixture are known; conversely, if the gene frequencies of a mixed population and of one of the original groups are known, it is possible to calculate the gene frequency of the other group.

Isolation has probably influenced the geographical distribution of genes from earliest times, when men were few and dispersed in small, sparsely scattered groups, up to the present day. As a result of isolation a gene may be lost to the isolated population by chance in the course of random mating. This is most likely to occur when the isolated population is small, it being understood that the breeding portion of a population, which is all that counts, is but a fraction of the total. In this way variations may arise in the gene frequencies of the populations, not only of continents, but of local geographical regions within continents, giving rise to differences within the species which have been designated by Dobzhansky as "micro-geographic races".

In 1940, when the work here reported was begun, although the frequencies of the A, B groups in various parts of Australia were known, there were many places where they were unknown, and the frequency of the M, N types was quite unknown to us. Shortly afterwards, Birdsell and Boyd (1940) published the results of their examination of the blood of 730 aborigines living principally in the coastal areas of Queensland and in the south-western and the Laverton-Warburton Range areas of Western Australia. Their results within the M, N system were so surprising that it was decided to continue our survey in parts of the continent not visited by them. Our investigation was curtailed by the war against Japan; but it seems desirable to place on record such data as we have been able to gather.

Materials and Methods.

Blood was taken from those aborigines who were selected as being pure blooded by our eleven collaborators; their names, the places where the specimens were collected and other data are shown in Table I. Birdsell (personal communication) has pointed out that some dark hybrids are indistinguishable even by the most scrupulous physical examination from pure-blooded aborigines. Our collaborators were aware of the importance of rejecting anyone who was suspected on any grounds of not being pure blooded; the results obtained justify confidence in their judgement on this essential point, to which further reference will be made later.

The frequency of the M, N types had not been examined in any locality where our specimens were taken. As is shown in Table I, however, the frequency of the A, B groups had been examined in several such places; probably some of our specimens at Woorabinda and Cherbourg (formerly Baramba) were taken from subjects tested by Birdsell in 1939, and it is possible that some at Cherbourg were from subjects tested by Tebbutt in 1923 or by Phillips in 1928, and that some at Oodnadatta or Alice Springs were subjects tested by Cleland in 1927.

In taking blood, the skin was thoroughly cleansed with ether before it was pricked, in order to reduce bacterial contamination of the specimen. A few drops of blood were received into one millilitre of sterile glucose-citrate solution (Rous and Turner, 1916) containing 0·001% (one in 100,000) "Merthiolate"; a small stoppered vial was used,

TABLE I.
Localities and Other Data.

Specimens Collected by.	Locality.	State.[1]	Number of Specimens.	Number of Tribes.	Days in Transit.	Remarks.
Dr. H. G. Dicks.	Port Hedland.	W.A.	16	9	4	None of these subjects was included in Gay's (1942) investigation of A, B groups. Practically all were unrelated.
Dr. K. R. Gay.	Broome.	W.A.	73	8	3	As for Port Hedland, above.
Mr. H. Ulrich.	Derby.	W.A.	26	9	2	Twenty subjects of the 26 were unrelated. No previous investigation here.
Dr. H. H. Wilson.	Wyndham.	W.A.	14	—	4	As for Broome, above.
Dr. W. B. Kirkland.	Darwin.	N.T.	99	42	4, 5	Leper hospital, 47; gaol, 29; remainder free. No previous investigation here.
Dr. W. B. Kirkland.	Bathurst and Melville Islands.	Off coast, N.T.	104	1	4	Tiwi tribe. Only 25 subjects of the 104 were unrelated. No previous investigation here.
Dr. J. H. Blackburn.	Woorabinda.	Q.	95	29	2	This settlement contains aborigines from all parts of Queensland. Birdsell (1940) examined 33 aborigines for A, B groups only.
Dr. St. A. W. L. McDowall.	Cherbourg (Baramba).	Q.	25	—	2	As for Woorabinda, above. Tebbutt (1923) examined 177 aborigines, Phillips (1928) examined 75, and Birdsell (1940) examined 42, for A, B groups only.
Dr. W. E. George.	Menindee.	N.S.W.	36	4	1	Only 10 subjects of the 36 were unrelated. No previous investigation here.
Mr. G. K. Bradey.	Oodnadatta.	S.A.	57	—	1	Cleland (1927) examined 19 aborigines for A, B groups only.
Dr. P. J. Reilly.	Alice Springs.	N.T.	104	9	2	Cleland (1927) examined 41 aborigines for A, B groups only.
Total.. ..	.. .. ..	.. ..	649	111[2]	—	——

[1] N.S.W. = New South Wales; W.A. = Western Australia; S.A. = South Australia; Q. = Queensland; N.T. = Northern Territory.
[2] There were actually 107 tribes, four being represented in two localities.

which was placed immediately within a watertight metal container in a large (2·5 litre) thermos flask containing ice, and sent to Melbourne by air. All the specimens, except those from Groote Eylandt (*vide infra*), were received at the laboratory in satisfactory condition and were examined within four days, except some of those received from Darwin, which were examined on the fifth day after collection. In every case ice was still present in the flask when it was received at our laboratory. Preliminary experiments showed that the results obtained with blood which had been taken in this way and kept chilled for as long as three weeks were identical with those obtained with fresh blood.

It was an advantage to be able to store the testing fluids under the best conditions and to examine the specimens in our own laboratory instead of in the field, in places where the temperature is generally higher than 90° F. Cleland (1931, 1933), working in a hot and dusty tent, obtained misleading results with blood which had been kept for only a few hours, and Birdsell felt obliged to disregard the results obtained at Cherbourg and Woorabinda with old M and N testing fluids.

Agglutinating Sera.

In the determination of the blood groups selected human sera of high titre were used. The A (anti-B) and the B (anti-A) sera each had a titre of 1/250; the O serum had a titre of 1/250 for group A cells and 1/150 for group B cells. The serum was used undiluted on slides or tiles.

For the recognition of the subgroups a serum from a group B donor, which had a high titre against A_1 cells, but a low titre against A_2 cells, was chosen and absorbed with A_2 cells. Examination by means of this absorbed serum of 307 specimens of blood of group A or AB, taken at random from the white population, showed that 250 (81·4%) were of group A_1 or A_1B and 57 (18·6%) were of group A_2 or A_2B; this gives an $A_2:A_1$ ratio of 0·228, which is similar to that found in northern European populations.

For the M, N typing the same testing fluids and the same technique were used as in the investigation into the frequency of the M, N types in a random sample of 1,000 of the white population (Simmons *et alii*, 1941). From the mathematical analysis of the results of this investigation it was inferred that these testing fluids were specific and that the technique was satisfactory.

Controls.

Fresh blood of each group, subgroup and type was taken from members of the laboratory staff and included in each of the eleven batches of unknown specimens to control the potency and specificity of the sera and testing fluids.

Control of the specific agglutinability of the aboriginal red cells as received could have been effected by the inclusion in each batch of known red cells of the several kinds which had been taken along with the unknown specimens. This was not done; but there is reason to believe that the specific agglutinability of the specimens was unchanged. By using serum from a donor of group AB as a check, we were able to demonstrate that some of the specimens received from Groote Eylandt were panagglutinable.

Results.

Frequency of the M, N Types.

The frequency of the M, N types is shown in Table II. According to the theory of Landsteiner and Levine that heredity of the M and N factors depends upon a single pair of allelomorphic genes, the relation $\sqrt{\frac{M}{V}} + \sqrt{\frac{N}{V}} = 1$ should hold, provided that the population is in genetic equilibrium in respect of these factors. In practice this relation cannot be expected to hold exactly and the deviation $D = 1 - \left(\sqrt{\frac{M}{V}} + \sqrt{\frac{N}{V}}\right)$ is shown in the eighth column of Table II. It is seen that D is less than its standard deviation (σ_D, ninth colum) in eight out of the 11 localities, and in no locality is it as much as twice its standard deviation.

When the results obtained in the various localities are combined, however, D is found to be 2·64 times its standard deviation. The value of χ^2 for the combined results is 7·5, which gives the significant figure of 0·006 for the probability (P, twelfth column) that chance alone is responsible for the observed difference. This discrepancy may be due either to technical errors or to inhomogeneity of the sample, or to both these causes. It seems desirable, therefore, first to look for evidence of errors in technique, which may have resulted from incompletely absorbed or weak testing fluids, by submitting our results to mathematical analysis. The statements indicated in the following discussion were derived from mathematical considerations which are discussed in the appendix, only the conclusions derived therefrom being referred to here. If the testing fluids were incompletely absorbed (Appendix A), D would be positive; in our results, however, D is negative. Moreover, the proportion of MN would be unduly high, whereas in our results it is low (37·3%). If the testing fluids were weak (Appendix B), D would be negative, as it is in this instance. But the testing fluids used were in fact so potent that strong specific agglutination occurred on slides

TABLE II.
Frequency of M, N Types.

1	2	3	4	5	6	7	8	9	10	11	12
Locality.	Number Tested.	Number and Percentage of Types.			Frequency of Genes.[1]		D	σ_D	D/σ_D	χ^2	P
		M	MN	N	m	n					
Port Hedland ..	16	0 (0)	4 (25·0)	12 (75·0)	0·125	0·875	+0·133	0·125	1·06	—	0·29
Broome	73	4 (5·5)	24 (32·9)	45 (61·6)	0·219	0·781	−0·019	0·059	0·32	0·04	0·85
Derby	26	2 (7·7)	8 (30·8)	16 (61·5)	0·231	0·769	−0·061	0·098	0·62	0·46	0·5
Wyndham	14	2 (14·3)	5 (37·7)	7 (50·0)	0·321	0·679	−0·085	0·134	0·63	0·46	0·5
Darwin	99	12 (12·1)	40 (40·4)	47 (47·5)	0·323	0·677	−0·037	0·050	0·78	0·58	0·45
Bathurst and Melville Islands ..	104	15 (14·4)	40 (38·5)	49 (47·1)	0·337	0·663	−0·065	0·049	1·33	2·0	0·15
Woorabinda	95	8 (8·4)	38 (40·0)	49 (51·6)	0·284	0·716	−0·008	0·051	0·16	0·03	0·85
Cherbourg (Baramba) ..	25	3 (12·0)	9 (36·0)	13 (52·0)	0·300	0·700	−0·067	0·100	0·67	0·51	0·5
Menindee	36	8 (22·2)	15 (41·7)	13 (36·1)	0·431	0·569	−0·071	0·083	0·86	0·8	0·4
Oodnadatta ..	57	2 (3·5)	11 (19·3)	44 (77·2)	0·132	0·868	−0·066	0·066	1·00	1·38	0·25
Alice Springs ..	104	16 (15·4)	48 (46·1)	40 (38·5)	0·385	0·615	−0·012	0·049	0·24	0·08	0·8
Total ..	649	72 (11·1)	242 (37·3)	335 (51·6)	0·297	0·703	−0·052	0·019	2·64	7·5	0·006

[1] The gene frequencies are calculated from the relations $m = \frac{2M + MN}{2V}$, $n = \frac{2N + MN}{2V}$, $D = 1 - \left(\sqrt{\frac{M}{V}} + \sqrt{\frac{N}{V}}\right)$, $\sigma_D = \frac{1}{2\sqrt{V}}$ where V = number tested.

$\chi^2 = \frac{(b^2 - 4ac)^2 V}{(2a + b)^2 (b + 2c)^2}$ where a, b and c = number of subjects of types M, MN and N respectively in a sample containing V subjects.

in less than fifteen minutes (Figure I), and no test result was read as negative until after thirty minutes. That the reading at thirty minutes did not differ from that at fifteen minutes is an indication of the strength and specificity of the testing fluids. Moreover, samples of blood of each type were included as controls in every test.

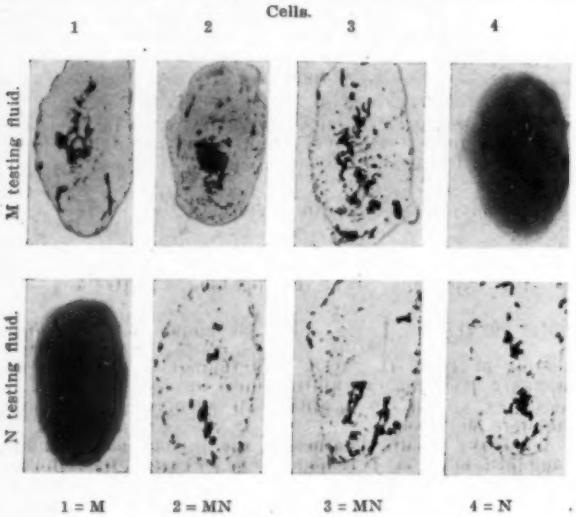


FIGURE I.

M and N slide agglutination at fifteen minutes. Raised lines of white paint were used to divide the slide. Equal parts of testing fluid and cell suspension were mixed and allowed to stand at room temperature in a moist chamber before examination. (In practice, the M and N testing fluids were placed on separate slides.)

The divergence from what was to be expected in the combined results is apparently not due therefore to errors in technique, but to lack of homogeneity of the samples examined. *D* should be negative in genetically heterogeneous populations (Appendix C). Ten of the eleven samples examined gave a negative value of *D*; although this is not individually significant because of the smallness of the samples, it is nevertheless suggestive that they were not within themselves homogeneous. This is possibly the result of including close kin in some of the groups. On the other hand the divergence from the expected result, which is apparent in the combined results, may also be due to real genetic differences between the various widely scattered and practically isolated communities from which some of our samples were drawn. If the χ^2 test is applied to the complete results, the probability is only 0·0235 that all the samples were taken from one basic population (not necessarily in genetic equilibrium).

Frequency of the A, B Groups.

The frequency of the A, B groups is shown in Table III. From this it appears that the A_2 and the B factors were entirely absent from the blood of the 649 subjects included in the table, whereas the relative frequency of A_1 and O varied widely in different localities.

Actually four specimens containing the B factor were received. One of these was obtained by Dr. W. B. Kirkland in Darwin from a man, aged forty-five years, of the Mainoru tribe, who was born in the Liverpool River district in Arnhem Land. (This, until about forty years ago, used to be visited regularly by trading vessels from the Celebes Islands.) This man possessed straight black hair and somewhat finer features than are usual in Australian aborigines, although not finer than are occasionally found in some pure-blooded Australians. Dr. Kirkland reexamined him, but was unable to elicit any genealogical information; he thought that the man's appearance indicated the probability of Indonesian admixture. There is, therefore, at least grave doubt as to his being pure blooded.

TABLE III.

Frequency of A, B Groups.

Locality.	Number Tested.	Number and Percentage of Groups.		Frequency of Genes.[1]	
		A_1.	O.	*p*.	*r*.
Port Hedland ..	16	10 (62·5)	6 (37·5)	0·388	0·612
Broome	73	30 (41·1)	43 (58·9)	0·233	0·767
Derby	26	9 (34·6)	17 (65·4)	0·191	0·809
Wyndham	14	2 (14·3)	12 (85·7)	0·074	0·926
Darwin	99	39 (39·4)	60 (60·6)	0·222	0·778
Bathurst and Melville Islands ..	104	33 (31·7)	71 (68·3)	0·174	0·826
Woorabinda	95	47 (49·5)	48 (50·5)	0·289	0·711
Cherbourg (Baramba)	25	6 (24·0)	19 (76·0)	0·128	0·872
Menindee	36	32 (88·9)	4 (11·1)	0·667	0·333
Oodnadatta ..	57	37 (64·9)	20 (35·1)	0·408	0·592
Alice Springs ..	104	40 (38·5)	64 (61·5)	0·216	0·784
Total	649	285 (43·9)	364 (56·1)	0·251	0·749

[1] In the absence of the B factor, the gene frequencies were derived simply from the equations $p = 1 - \sqrt{o}$, $r = \sqrt{o}$.

The remaining three specimens were obtained by Dr. J. H. Blackburn at Woorabinda from subjects who were afterwards found on genealogical evidence to be hybrids.

The absence of B from our samples and the dominance of the gene for A over the gene for O render it impossible to submit the results to the usual statistical tests.

The Subgroups.

The 293 aborigines of group A, including the eight found on Groote Eylandt, all belonged to the subgroup A_1.

Groote Eylandt.

The Reverend L. J. Harris, Acting Superintendent of the Mission Station on Groote Eylandt, with some difficulty generously collected and forwarded to Melbourne specimens from 83 aborigines living on the island. Unfortunately, 61 of the specimens were fourteen to eighteen days old when they were received; although they had been kept in a refrigerator, many were contaminated by bacteria and lysed, and nine showed the Hubener-Thomsen phenomenon of pan-agglutination (Wiener, 1939). Organisms isolated from these nine specimens (Gram-positive bacilli and cocci) were found to be capable of reproducing the phenomenon in fresh blood. The remaining 22 specimens were received after ten days; the thermos flask contained ice when it was opened, there was no hæmolysis and the agglutination reactions seemed satisfactory; but owing to the doubt which must be attached to them, these specimens have been excluded from the main series. Owing to the war it was impossible to repeat this work, and since the opportunity to do so may

TABLE IV.

Groote Eylandt.

Number Tested.	Frequency of A, B Groups.				Frequency of M, N Types.					D/σ_D.
	Number and Percentage of Groups.		Frequency of Genes.		Number and Percentage of Types.			Frequency of Genes.		
	A_1	O	*p*	*r*	M	MN	N	*m*	*n*	
54	8 (14·8)	46 (85·2)	0·077	0·923	3 (5·6)	19 (35·2)	32 (59·3)	0·231	0·769	0·09

never recur, the results are shown in Table IV. Thirty-two specimens of the first batch were tested, all of the second batch. All the aborigines (except two in the first batch) were natives of Groote Eylandt or of the adjacent islands; the remaining two were born in the River Rose district in the Northern Territory. Many of the first batch, but only two of the second, were kinsmen.

Discussion.

Field observations have led Birdsell and Boyd to conclude that the Australian aborigines are not a homogeneous people, although this conclusion was not confirmed by the blood-group frequencies within their sample. Our own results cannot be accepted as conclusive evidence of inhomogeneity, because a number of kinsmen was included in some of our samples. Quite possibly, too, a few dark hybrids (see above) were included; but we do not believe that these were so numerous as to cause our samples to differ significantly from one truly representative of the population. The absence of B and of A_2 from the blood of more than 700 aborigines examined lends support to this belief, as also does the similarity of our results with those of the trained anthropologists who had the opportunity of selecting the subjects comprising their samples on genealogical as well as on physical evidence.

Within the M, N system our results agree with those of Birdsell and Boyd, in the finding of the frequency of gene *n* to be much higher than has been reported for any other people. The highest frequency of *n* (0·564) previously known occurred among the Ainu (Kubo, 1936), descendants of a people closely related to, if not identical with, the neolithic inhabitants of Japan.

Work is now in progress to ascertain the frequencies of the M, N types of blood samples from natives of Indonesia and Melanesia, which lie upon the route followed by early immigrants from eastern Asia to Australia.

Birdsell and Boyd have mapped isogenes (lines of equal gene frequency) based not only on their blood-group data, but also on other anthropological data. In Figure II are shown their isogenes for the gene *n* and additional isogenes based on our own results in areas not visited by them. The

FIGURE II.

Approximate positions of lines of equal frequency of gene *n*. The continuous lines are those of Birdsell and Boyd. The interrupted lines are based upon our own data.

area of highest incidence of M (lowest of N) is centred in the Northern Territory; the incidence decreases to the west, south and east of this centre. If the blood of early inhabitants of Australia was of very high N, it is not unlikely that during their long isolation the *m* gene was lost from parts of the continent, as it appears to have been lost from the Laverton-Warburton Range area.

Birdsell and Boyd have suggested that there existed during the Pleistocene a north-to-south gradient of N in eastern Asia, citing as evidence of this the low frequencies of N in North America and the high frequencies in Australia. The intermediate frequencies which one might expect to find in Asia have been obliterated by later migrations (mixture) on the Asiatic mainland. The Australian figures, many of which are statistically small, however, which show a progressive increase in the frequency of N radiating outwards from the north-west over the continent, fit in nicely with this suggestion. However, it does not seem likely that the variations of N found within Australia could have persisted for so long; it seems more likely that these variations are the result of later immigrations and of isolation within the continent.

There was no significant difference ($P = 0{\cdot}25$) in our samples between the M, N frequencies of coastal and inland areas corresponding to that found in the A, B groups.

Within the A, B system, the absence of A_2, the rarity of the B factor and the variation in the relative frequencies of A and O are remarkable.

The subgroups of A are inherited according to simple genetic laws, but little is known at present of their geographical distribution. It is interesting to note, however, that the subgroup A_2 is absent from American Indians (Landsteiner *et alii*, 1942; Matson *et alii*, 1936), the Hawaiians (Nigg, 1930) and the Australian aborigines, and that it is rare in the Eskimos and the Chinese. Of the races so far examined, its frequency is appreciable only in the white races and Negroes.

Cleland did not find one subject possessing the B factor among 776 examined by him in central and southern Australia. In only 62 instances has it been recorded among more than 3,000 apparently pure-blooded aborigines examined. These are discussed in detail by Birdsell and Boyd, who found seventeen pure-blooded aborigines of group B; they agree with Cleland in holding that some slight recent infiltration by the B factor has occurred in the far north of the continent. Practically all of the apparently pure-blooded aborigines in whom the B factor has been found originated there. The subject of group B, whom, in view of the doubt expressed by Dr. Kirkland, we have excluded from our series, was born in Arnhem Land. If the hypothesis of Cleland and of Birdsell and Boyd is correct, the absence of the B factor from Cleland's large sample is not surprising; but it is surprising that it was absent from the 653 aborigines examined by Gay (1942) and by us in the north, north-east and north-west coastal areas, where, according to their hypothesis, all those possessing the B factor were born. (Many of those in our samples at Cherbourg and Woorabinda were born in the north.) This absence may indicate that infiltration by the B factor is more recent and more restricted than had been thought. It appears that the B factor has penetrated no further than Cape York Peninsula, which was probably its point of entry from the nearby islands of Melanesia. In Figure II a line of crosses and circles indicates the extent to which we believe that it had penetrated before the advent of the white man. More work is needed before the significance of the rare B factor occurring in the north of Australia can be assessed in relation to its frequency in the inhabitants of the neighbouring Pacific islands, who, until prohibited in 1904, were frequent visitors to the northern coast. More recently Japanese vessels have also traded along the coast; however, the oldest Japanese hybrid noticed on Bathurst and Melville Islands by Ford (1942), who medically examined 571 aborigines there, was aged only nine years.

In Table V, which should be studied together with Figure III, are shown all numerically important published results of those who have examined the blood groups within the A, B system. Although some of the samples examined were small, the results obtained by different investigators in the same localities are generally similar. The widest discrepancy is that found between the results obtained at Cherbourg (Baramba) by Phillips (1928) and Tebbutt (1923), which agree within sampling error, and those obtained at the same place by Birdsell and Boyd (1940), who found $p = 0{\cdot}090$, $q = 0{\cdot}027$ and $r = 0{\cdot}888$, and ourselves (Table III). The last-mentioned two samples were small—only 42 and 25 respectively—and this may account for the discrepancy; moreover, in view of the high

TABLE V.

Results obtained by Various Authors Arranged in Order of the Frequency of p (the Gene for A) to show the General Trend of the Geographical Distribution of the A (and B) Factor in Australia.

Author.	Locality.	Number Tested.	Percentage of Groups.				Frequency of Genes.[1]			D/σ_D.
			O	A	B	AB	*p*	*q*	*r*	
Peripheral (Coastal) Areas:										
Birdsell	Palm Island, Queensland.	137	63·5	32·1	4·4	0	0·176	0·022	0·797	1·2
Lee	Palm Island, Queensland.	377	60·3	31·7	6·4	1·6	0·183	0·041	0·777	0·3
Birdsell	Yarrabah, Queensland.	101	62·4	33·7	4·0	0	0·185	0·020	0·790	1·0
Phillips	Cherbourg (Baramba), Queensland.	75	52·0	37·3	10·7	0	0·208	0·055	0·721	1·6
Birdsell	Monamona, Queensland.	96	58·3	37·5	4·2	0	0·209	0·021	0·764	1·1
Tebbutt	Cherbourg (Baramba), Queensland.	177	55·9	37·3	6·2	0·6	0·212	0·035	0·748	1·0
Gay	North-west (Kimberley) area of Western Australia.	201	61·2	38·8	0	0	0·218	0	0·782	—
Present Authors ..	Coastal areas of Queensland, Northern Territory and north-west of Western Australia.	452	61·1	38·9	0	0	0·218	0	0·782	—
Birdsell	South-west area of Western Australia.	106	51·9	48·1	0	0	0·280	0	0·720	—
Central (Inland) Areas:										
Present Authors ..	Inland areas, Menindee, Oodnadatta, Alice Springs.	197	44·7	55·3	0	0	0·331	0	0·669	—
Birdsell	Laverton - Warburton Range Area, Western Australia.	102	43·1	56·9	0	0	0·343	0	0·657	—
Cleland	Combined results of many investigations. Eight-ninths of the subjects examined were in the inland areas of Northern Territory and South Australia.	774	38·5	61·5	0	0	0·380	0	0·620	—

[1] The gene frequencies are calculated from the relations $p = 1 - \sqrt{\frac{O+B}{100}}$, $q = 1 - \sqrt{\frac{O+A}{100}}$, $r = \sqrt{\frac{O}{100}}$. $D = 1 - (p + q + r)$.

$\sigma_D = \sqrt{\frac{pq}{2V(1-p)(1-q)}}$ where V is the total number of individuals in each sample.

q incidence in the two larger samples, it is possible that they included some dark hybrids. Gay's (1942) results for a north-western coastal area are identical with ours for north-western, northern and north-eastern coastal localities.

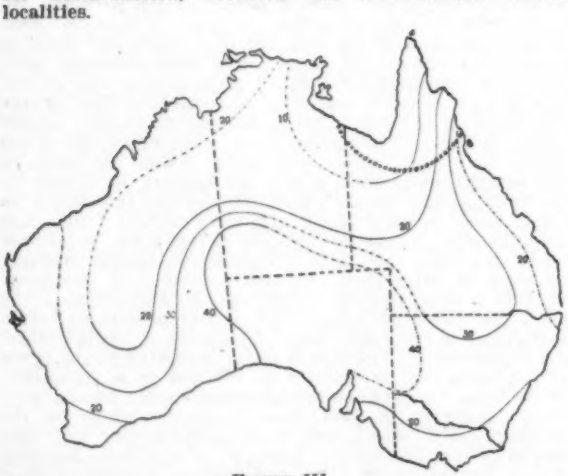


FIGURE III.

Approximate positions of lines of equal frequency of gene *p* based upon data presented in Table V. The continuous lines are those of Birdsell and Boyd. The interrupted lines are based upon our own and Gay's data. The line of crosses and circles delimits the probable area of penetration by the B factor before the arrival of the white races.

The results in Table V are arranged in order of the frequency of *p* (the gene for A), so as to show the general trend of the geographical distribution of the gene *p* in Australia. The distribution of the B factor (gene *q*) has already been discussed. There is a wide variation in the relative frequencies of *p* and *r* (the gene for O) in different localities; our own figures reveal a significant difference between the frequencies for peripheral (coastal) as compared with central (inland) localities ($P < 0{\cdot}001$, $\chi^2 = 15{\cdot}0$); this is in accord with that shown in the results of others. Birdsell and Boyd have mapped isogenes of *p*, based on their recent work and on the earlier work of others, by means of which are shown a nuclear area of high *p* in central Australia and regions of lower *p* towards the coast. Gay's results and our own in the north-west and north have made it possible to complete the map

FIGURE IV.

Places in block letters are areas of investigation by the present authors; places in small letters are areas of investigation by other authors (see Table V). Shaded area (horizontal) is Kimberley district (Gay, 1942). Cross-hatched areas with index numbers in centre are areas visited by Cleland and his collaborators (1926-1938). 1 = Point McLeay (1926, 1930); 2 = north-east of South Australia, Innamincka (1926); 3 = Murnpeowie (1926); 4 = Tarcoola district (1926); 5 = Macumba River district (1927); 6 = Alice Springs (1927); 7 = Point Pearce (1929); 8 = Konnibba and Penong (1929); 9 = Hermannsburg Mission (1930); 10 = Macdonald Downs (1931); 11 = Cockatoo Creek (1932); 12 = Mount Liebig (1933); 13 = Musgrave Ranges (1936); 14 = Diamantina district (1936); 15 = Granites Goldfield (1938); 16 = Flinders Range (north) (1938).

(Figure II), which is based upon the data shown in Table V.

TABLE VI.

Occurrence of the Blood-Groups in Some Populations which Probably Migrated from Eastern Asia, as Compared with those of the Ainu and of Other Populations.

Race.	A_1.	A_2.	B.	O.	M.[1]	N.
Ainu	(+)[2]		+[2]	+	18%	32%
Indonesians	(+)		+	+	?[3]	?
Micronesians	(+)		+	+		
Melanesians	(+)		+	+		
Polynesians:						
Maoris	(+)		Very rare.	+		
Samoans	(+)		+	+		
Hawaiians	+	−[2]	Rare.	+		
Australian Aborigines	+	−	Very rare.	+	10%	50%
North American Indians	+	−	Very rare.	+	60%	5%
Eskimos	+	Very rare.	Moderate.	+	66–83%	2%
Chinese	+	Very rare.	+	+	33%	18%
Other populations	+	+	+	+	30%	20%

[1] The M, N percentages are approximate.
[2] (+) = not differentiated, + = present, − = absent.
[3] The M, N figures of Postmus for Indonesia are regarded as being statistically unreliable and are not quoted.

In our map we have retained Birdsell and Boyd's isogenes as far as possible and have made the minimal alterations consistent with the additional figures now available. We have extended their nuclear area of high p into New South Wales, because our highest value (p = 0·67) was obtained there, though admittedly from a small sample. Incidentally, Birdsell and Boyd from a different small sample obtained their highest p frequency in New South Wales (p = 0·622). The chief additions and alterations to their map are in the north and the north-west, where new data are available.

The significant differences in the relative frequencies of A and O within Australia would seem to be attributable principally to geographical isolation of small communities within the continent. The same hypothesis has been put forward by Landsteiner *et alii* (1942) to account for the wide variation in the frequency of A and O among the North American Indians, who, like the Australian aborigines, show an absence or extreme rarity of group B, but exhibit, in contrast to the Australians, a very low frequency of N. The absence of the subgroup A_2 in both of these races emphasizes still further the similarity in regard to the A, B groups in the blood of the aboriginal inhabitants of these two widely separated continents. These points are brought out in Table VI, which also shows broadly the geographical distribution of the genes for the blood groups in some of the areas which are believed to have been populated by migrants from eastern Asia, as compared with those for the blood groups of the Ainu, an aboriginal population of Japan, and for all other populations.

It is not surprising that, in a continent so isolated and so sparsely populated for so many thousands of years as Australia, unusual and variable gene frequencies should be found. The singularly high N frequency, the complete absence of A_2 and the absence of B from all but a very small fraction of the continent may thus be accounted for. It appears that the inhabitants of south-eastern Asia, whence the Australian aborigines, the Polynesians and the North American Indians are believed to have migrated, lacked the B factor and probably the A_2 factor. The B factor was introduced to south-eastern Asia after these migrations, whence it has spread through Indonesia and Melanesia, stopping short of Australia and western Polynesia.

Summary.

The blood of 703 Australian aborigines has been grouped within the M, N and A, B systems. The sample was drawn from three central (inland) districts and from eight peripheral (coastal) districts on the north-west, north and north-east coasts and adjacent islands.

A singularly high frequency of N was found; this finding confirms the work of Birdsell and Boyd.

The blood of all of 293 subjects of group A belonged to the subgroup A_1.

The B factor was absent from the sample. The frequency of A and O varied in different localities, and a significant difference was observed in the relative frequencies of A and O among aborigines from peripheral (coastal) areas as compared with central (inland) areas. This difference has been correlated with the various frequencies observed by other workers.

The significance of the results in relation to the ethnology of the Australian aborigine is discussed.

Acknowledgements.

We are greatly indebted to our collaborators, who freely bore the burden and heat of the day in collecting the specimens in the field; we are indebted also to those who kindly arranged transport, and to Mr. G. Anderson, B.Sc., for his helpful criticism.

Bibliography.

J. B. Birdsell and W. C. Boyd: "Blood Groups in Australian Aborigines", *The American Journal of Physical Anthropology*, Volume XXVII, June 29, 1940, page 69.

W. C. Boyd: "Blood Groups", *Tabulæ Biologicæ*, Volume XVII, 1939, page 113; "Critique of Methods of Classifying Mankind", *The American Journal of Physical Anthropology*, Volume XXVII, 1940, page 333.

J. B. Cleland: "Blood Grouping of Australian Aboriginals", *The Australian Journal of Experimental Biology and Medical Science*, Volume III, 1926, page 33; "Blood-grouping of Australian Aboriginals at Oodnadatta and Alice Springs", *Transactions of the Royal Society of South Australia*, Volume LI, 1927, page 78; "Further Results in Blood Grouping Central Australian Aborigines", *The Australian Journal of Experimental Biology and Medical Science*, Volume VII, 1930, page 79; "The Blood Grouping of Central Australian Aborigines, 1930 Series", *The Journal of Tropical Medicine and Hygiene*, Volume XXXIV, November 21, 1931, page 353; "The Blood Grouping of Central Australian Aborigines, 1931 Series", *The Journal of Tropical Medicine and Hygiene*, Volume XXXV, December 15, 1932, page 369; "Blood Grouping of Central Australian Aborigines, 1932 Series", *The Journal of Tropical Medicine and Hygiene*, Volume XXXVI, December 15, 1933, page 377.

J. B. Cleland, C. Hackett and T. H. Johnston: "Blood Grouping of Aborigines of the Musgrave Ranges in the North-west of South Australia", *The Journal of Tropical Medicine and Hygiene*, Volume XXXIX, February 1, 1936, page 25.

J. B. Cleland and T. H. Johnston: "Blood Grouping of Aborigines of the Diamantina District in the North-east of South Australia: 1934 Series", *The Journal of Tropical Medicine and Hygiene*, Volume XXXIX, May 1, 1936, page 104; "Blood Grouping of Aborigines in the North-west Portion of Central Australia: 1936 Series", *The Journal of Tropical Medicine and Hygiene*, Volume XLI, January 1, 1938, page 10; "Blood Grouping of Aborigines of the Northern Flinders Ranges in South Australia (1937 Series)", *The Journal of Tropical Medicine and Hygiene*, Volume XLI, January 15, 1938, page 26.

J. B. Cleland and H. H. Woollard: "Further Results in the Blood Grouping of South Australian Aborigines", THE MEDICAL JOURNAL OF AUSTRALIA, July 6, 1929, page 2.

T. Dobzhansky: "Genetics and the Origin of Species", 1937.

E. Ford: "Medical Conditions on Bathurst and Melville Islands", THE MEDICAL JOURNAL OF AUSTRALIA, September 12, 1942, page 235.

R. K. Gay: "Blood Grouping of Aborigines of North-West Australia", THE MEDICAL JOURNAL OF AUSTRALIA, November 14, 1942, page 435.

J. B. S. Haldane: "The Blood-group Frequencies of European Peoples and Racial Origins", *Human Biology*, Volume XII, 1940, page 457.

L. Hirschfeld and H. Hirschfeld: "Serological Differences between the Blood of Different Races", *The Lancet*, Volume II, 1919, page 675.

T. Kubo: "On the Agglutinogens M and N of the Ainu", *The Journal of Immunology*, Volume XXX, 1936, page 287.

K. Landsteiner, A. S. Wiener and G. A. Matson: "Distribution of Rh Factor in American Indians", *The Journal of Experimental Medicine*, Volume LXXVI, July, 1942, page 73.

D. H. K. Lee: "Blood Groups of North Queensland Aborigines, with a Statistical Collection of Some Published Figures for Various Races", THE MEDICAL JOURNAL OF AUSTRALIA, September 25, 1926, page 401.

D. J. Mahony: "The Problem of Antiquity of Man in Australia", *Memoirs of the National Museum, Melbourne*, Volume XIII, 1943, page 7.

G. A. Matson, P. Levine and H. F. Schrader: "Distribution of the Subgroups of A and the M and N Agglutinogens among the Blackfeet Indians", *Proceedings of the Society for Experimental Biology and Medicine*, Volume XXXV, 1936-1937, page 46.

C. Nigg: "A Study of the Blood Group Distribution among Polynesians", *The Journal of Immunology*, Volume XIX, 1930, page 93.

G. Phillips: "The Blood Groups of Full-Blood Australian Aborigines", THE MEDICAL JOURNAL OF AUSTRALIA, September 8, 1928, page 296.

P. Rous and J. R. Turner: "The Preservation of Living Red Blood Cells in Vitro", *The Journal of Experimental Medicine*, Volume XXIII, 1916, page 219.

P. Schiff and W. C. Boyd: "Blood Grouping Technic", 1942.

R. T. Simmons, L. M. Bryce, J. J. Graydon and H. Wilson: "A Note on the Preparation and Use of M and N Testing Fluids", THE MEDICAL JOURNAL OF AUSTRALIA, October 25, 1941, page 474.

A. H. Tebbutt: "Comparative Iso-Agglutinin Index of Australian Aborigines and Australians", THE MEDICAL JOURNAL OF AUSTRALIA, September 29, 1923, page 396.

N. B. Tindale and J. B. Birdsell: "Tasmanoid Tribes in North Queensland", *Records of the South Australian Museum*, Volume VII, Number 1, 1942, page 1.

A. S. Wiener: "Blood Groups and Blood Transfusion", Second Edition, 1939, page 37.

Appendix.

(J.J.G.)

When a population is in genetic equilibrium, the relation $\sqrt{M}+\sqrt{N}=1$ should hold within the limits of the error of sampling. Actually, in any series $\sqrt{M}+\sqrt{N}$ will differ from 1 by an amount D, whose standard error is given by $\sigma_D=\frac{1}{2\sqrt{V}}$, where V is the total number of samples examined (Wiener, 1931).

If chance sampling errors alone were present, positive and negative values of D would be equally likely. However, other factors cause systematic changes in the equation $D=1-(\sqrt{M}+\sqrt{N})$, some tending to produce negative values for D and others positive values for D.

The effects of some of these factors are examined below.

(*A*) *The Effect of Incompletely-absorbed Sera.*

The effect of incompletely-absorbed sera is to increase the number of samples classified as MN at the expense of those classified as M or N. So that if

M, MN, and N represent the true frequencies of the types, and

M′, MN′, and N′ represent the observed frequencies of the types,

then $\sqrt{M'}+\sqrt{N'}$ will be less than $\sqrt{M}+\sqrt{N}$, but $\sqrt{M}+\sqrt{N}=1$

Hence D, which equals $1-(\sqrt{M'}+\sqrt{N'})$, will be positive.

(*B*) *The Effect of Weak Sera.*

When weak sera are used, some positive reactions may be missed; but because no blood samples are classified as lacking in both genes, the samples not correctly classified will all belong to type MN. These samples will be wrongly classified either as type M or as type N, and so $\sqrt{M'}+\sqrt{N'}$ will be greater than $\sqrt{M}+\sqrt{N}$. Hence D will tend to be negative if either of the sera used is weak.

(*C*) *Heterogeneity.*

Consider a heterogeneous population as being a mixture of several homogeneous populations, for each of which the relation $m+n=1$ holds. Let the populations be classified as follow:

(1) P_1 individuals with frequency of types M_1, MN_1 and N_1, and of genes m_1 and n_1.

(2) P_2 individuals with frequency of types M_2, MN_2 and N_2, and of genes m_2 and n_2.

(3) P_3 individuals with frequency of types M_3, MN_3 and N_3, and of genes m_3 and n_3

and so on.

Then $M_1=m_1^2$, $MN_1=2m_1n_1$ and $N_1=n_1^2$ *et cetera.*

The true frequency of the gene for M in the mixed population will be the weighted average of the separate frequencies of the M gene, that is,

$$m=\frac{P_1m_1+P_2m_2+P_3m_3+\ldots}{P_1+P_2+P_3+\ldots}$$

Hence

$$m^2=\frac{P_1^2m_1^2+P_2^2m_2^2+P_3^2m_3^2+\ldots+2P_1P_2m_1m_2+\ldots}{(P_1+P_2+P_3+\ldots)^2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\text{(i)}$$

The observed frequency of type M is the sum of that type in each of the separate populations divided by the total individuals in all groups, that is,

$$M'=\frac{P_1m_1^2+P_2m_2^2+P_3m_3^2+\ldots}{(P_1+P_2+P_3+\ldots)} \text{ for } M_1=P_1m_1^2 \quad \ldots\ldots\ldots\ldots\ldots\ldots\text{(ii)}$$

If the denominator and numerator of (ii) are each multiplied by ΣP_1 we get

$$M'=\frac{P_1(P_1+P_2+P_3+\ldots)m_1^2+P_2(P_1+P_2+P_3+\ldots)m_2^2+P_3(P_1+P_2+P_3+\ldots)m_3^2+\ldots}{(P_1+P_2+P_3+\ldots)^2} \quad \ldots\ldots\ldots\ldots\ldots\ldots\text{(iii)}$$

From (i) and (iii)

$$M'-m^2=\frac{P_1(P_2+P_3+\ldots)m_1^2+P_2(P_1+P_3+\ldots)m_2^2+P_3(P_1+P_2+P_4+\ldots)m_3^2+\ldots-2P_1P_2m_1m_2-\ldots}{(P_1+P_2+P_3+\ldots)^2}$$

$$=\frac{P_1P_2(m_1^2+m_2^2-2m_1m_2)+P_1P_3(m_1^2+m_3^2-2m_1m_3)+\ldots}{(P_1+P_2+P_3+\ldots)^2}$$

$$=\frac{P_1P_2(m_1-m_2)^2+P_1P_3(m_1-m_3)^2+\ldots P_2P_3(m_2-m_3)^2+\ldots}{(P_1+P_2+P_3+\ldots)^2}$$

All the terms of the numerator are either positive or zero.

Hence $M'>m^2$ or $\sqrt{M'}>m$.

Similarly $\sqrt{N'}>n$

but $m+n=1$

$\sqrt{M'}+\sqrt{N'}>1$

and D, which equals $1-(\sqrt{M'}+\sqrt{N'})$, is therefore negative.

Thus the heterogeneity resulting from the mixture of homogeneous groups with different gene frequencies tends to produce a negative value for D.

(*D*) *Inbreeding.*[1]

Suppose the true underlying frequencies of the M and N genes are m and n, and that when one parent provides (say) gene factor M, then the chances of the second factor's being M or N are m_x and n_x respectively instead of m and n. Similarly, when the first gene factor is N, let the chances of the second factor's being M or N be m_y and n_y respectively.

Then frequency of $MM=m\,.\,m_x$ and of $NN=n\,.\,n_y$

and the frequency of $MN=m\,.\,n_x+n\,.\,m_y$.

The chance of getting the M factor from the first parent and the N factor from the second is the same as the chance of getting the N factor from the first parent and the M factor from the second.

Therefore $m\,.\,n_x=n\,.\,m_y$

or $\frac{m_y}{m}=\frac{n_x}{n}=1-\alpha$, say;

α is suggested as the "coefficient of inbreeding" by Bernstein.

[1] F. Bernstein: *"Ueber die Erblichkeit der Blutgruppen"*, *Zeitschrift für induktive Abstammungs und Vererbungslehre*, Volume LIV, 1930, page 400; *"Fortgesetzte Untersuchungen aus den Theorie der Blutgruppen"*, *ibidem*, Volume LVI, 1930, page 233. A. S. Wiener: "Heredity of Agglutinogens M and N of Landsteiner and Levine: Theoretico-Statistical Considerations", *The Journal of Immunology*, Volume XXI, 1931, page 157.

Now $m_x+n_x=1$.

Thus $m_x=1-n_x=1-(1-\alpha)n=1-(1-\alpha)+(1-\alpha)m$
$=\alpha+(1-\alpha)m$

Hence the frequency of $MM=m\,.\,m_x=\alpha m+(1-\alpha)m^2$ .....(iv)

Similarly the frequency of $NN=n\,.\,n_y=\alpha n+(1-\alpha)n^2$ and the frequency of $MN=m\,.\,n_x+n\,.\,m_y=(1-\alpha)mn+(1-\alpha)mn$
$=2(1-\alpha)mn$.

Now $MM+\frac{MN}{2}=\alpha m+(1-\alpha)m^2+(1-\alpha)mn$
$=\alpha m+(1-\alpha)m(m+n)$, but $m+n=1$
$=\alpha m+(1-\alpha)m$
$=m$.

Similarly $NN+\frac{MN}{2}=n$.

The expression $\frac{\frac{MN}{2}}{\left(MM+\frac{MN}{2}\right)\left(NN+\frac{MN}{2}\right)}=\frac{(1-\alpha)mn}{m\,.\,n}=1-\alpha$

from which α may be calculated from a knowledge of the group frequencies.

The coefficient α may vary from -1 to $+1$.

When $\alpha=-1$ only heterozygotes appear in the population and $m=n=\frac{1}{2}$.

Some laws of marriage tend to reduce breeding within groups and so produce a negative value for α.

When $\alpha=0$, the population is homogeneous and

$MM=m^2$, $NN=n^2$ and $MN=2mn$.

When $\alpha=1$ only homozygotes appear in the population and there is complete inbreeding. Though nothing approaching complete inbreeding is found in practice, there is in many cases a real tendency to inbreeding due to isolation, and the effect of this on D may be seen in the following.

From (iv) MM (or M′)$=\alpha m+(1-\alpha)m^2$
$=m^2+\alpha m(1-m)$
$=m^2+\alpha mn$
$=m^2\left(1+\frac{\alpha n}{m}\right)$ .....(v)

Hence $\sqrt{M'}>m$, if $\alpha>0$

Similarly $\sqrt{N'}>n$.

Hence D tends to be negative under the influence of inbreeding.

From (v) $\sqrt{M'}=m\left(1+\frac{\alpha n}{2m}-\frac{\alpha^2n^2}{8m^2}+\frac{\alpha^3n^3}{16m^3}-\ldots\right)$

and $\sqrt{N'}=n\left(1+\frac{\alpha m}{2n}-\frac{\alpha^2m^2}{8n^2}+\frac{\alpha^3m^3}{16n^3}-\ldots\right)$

From which $D=1-(m+n)-\frac{\alpha}{2}(m+n)$ neglecting higher order terms of α.

D is approximately equal to $-\frac{\alpha}{2}$.

If technical errors are insignificant then D (or α) is really an easily calculated coefficient of inhomogeneity of the sample tested.

RECENT ADVANCES IN THE TREATMENT OF CARCINOMA OF THE PROSTATE.[1]

By D. COLEMAN TRAINOR, M.B., Ch.M., F.R.C.S.E.,

Honorary Urologist, Royal South Sydney Hospital;
Honorary Assistant Urologist, Lewisham Hospital;
Honorary Consulting Urologist, St. Margaret's Hospital, Sydney.

THE hormonal treatment of cancer of the prostate is one of the outstanding achievements of this century, and ranks in importance with the discovery of the sulphonamide drugs and penicillin. Not only has a better understanding of hormonal influence on prostatic cancer placed in our hands a method of relieving the symptoms of one of the most distressing of all forms of cancer, but the establishment of a relationship between cancer and its control by synthetic hormones should give renewed impetus to research along these lines in cancer generally.

Fifty years ago men with enlarged prostates were treated empirically by castration, and the condition of a certain number of them improved. Those whose condition improved most presumably had carcinoma of the prostate.

Please note the phrase "relieve the symptoms", for it is too early yet to claim any cures. For one thing, a sufficient length of time has scarcely elapsed since this treatment came into general use, and apart from this, no case has yet been reported in which cure could be reasonably regarded as having been achieved. The results of hormonal treatment are gratifying and even dramatic, but if the hormonal imbalance is allowed to recur, so will the symptoms of the cancer. A large literature is arising from this new therapy; but I believe that the object of this paper will be best served by confining it to known facts and avoiding academic speculation. It will be confined, therefore, to a discussion of the principles involved and their practical application.

There exists in the body a balance between the male and female hormones, androgen and œstrogen. In health they work in harmonious antagonism. Their effects on the prostate have been shown by a series of ingenious experiments by Huggins and Clark.[1] These workers isolated the prostate of dogs in such a way that the secretion of the prostate could be obtained in a pure form. They found that administration of testosterone caused increased prostatic activity as evidenced by an increased amount of secretion. When the administration of testosterone was discontinued and was replaced by administration of stilbœstrol, the secreting activity of the prostate was much lowered.

Testosterone is found also to produce proliferation of the prostatic epithelium,[2] and in excessive amounts this proliferation goes on to actual metaplasia. When testosterone is withdrawn, as by castration, or when its action is more than counter-balanced by the administration of stilbœstrol, the reverse process takes place and regressive changes in the prostate occur. It is interesting to note in this connexion that the sex hormones bear a striking resemblance in chemical structure to that of certain of the carcinoma-producing hydrocarbons produced from tar.[3]

Certain side effects also occur in some instances, such as increase in the size of the breasts, painful nipples and flushing of the face, due to a vasomotor disturbance similar to that noted in women at the climacteric. Œdema of the legs and ankles also occurs occasionally.

Let me now leave the discussion of the hormones for a moment to consider the enzyme known as phosphatase. This is an enzyme which has the power of splitting organic phosphorus compounds to give free phosphorus ions.[4][5] Phosphatase is designated as acid or alkaline according to whether it exhibits its optimum activity in acid or alkaline media. This enzyme occurs in large amounts in the prostate. It is present only in very small quantities up to the age of puberty, after which the quantity increases. It is present in its maximum quantities between the ages of twenty and forty years; after this time it decreases as the years advance. The technique of evaluating the quantities of phosphatase in the blood has been worked out by King and Armstrong, and the reading is usually given as so many King-Armstrong units. Acid phosphatase is more regular in its behaviour than the alkaline variety, and for that reason its concentration in the blood is used as an index of carcinomatous activity. The normal value of acid phosphatase in the blood is from 0·5 to 2·0 King-Armstrong units.

When a prostatic carcinoma has broken its capsule, and more particularly when it has metastasized, there is a sharp rise in the acid phosphatase concentration in the blood. This rise does not occur in other diseases of the prostate, but it does sometimes occur in advanced Paget's disease. The rise in the blood phosphatase level is strongly suggestive of a prostatic carcinoma, and if the rise is to above 2·5 King-Armstrong units, metastases should be strongly suspected. The reverse, however, does not always

[1] Read at a meeting of the Clinical Society, South Coast Medical Association, on July 22, 1944, at Wollongong.

hold good, and a normal or low blood phosphatase level should never be taken as evidence against carcinoma in the face of clinical signs. The reason for the rise in blood phosphatase level is that when the prostatic carcinoma has broken its capsule or metastasized, this substance enters directly into the blood stream.

In carcinoma of the prostate, administration of œstrogen or castration causes as a rule a pronounced lowering in its concentration. Not only, therefore, does the blood phosphatase level help us to assess the activity of the carcinoma, but its fall under œstrogen therapy gives an index of how effective the treatment is. The administration of androgen to a patient suffering from carcinoma of the prostate causes a pronounced rise, which again indicates that androgen stimulates the activity of the growth.

Stilbœstrol is considered to act on the prostate in one of the four following ways:[3] (*a*) it may act directly on the prostatic epithelium; (*b*) it may inactivate androgen; (*c*) it may depress the gonadotropic hormones of the anterior pituitary; (*d*) it may depress the interstitial cells of the testis.

Clinically, the effects of the withdrawal of androgen, as by castration, or of androgen neutralization by the administration of stilbœstrol, produces the following results. There is a great improvement in the patient's general condition. Appetite improves, and the general health is rapidly and strikingly ameliorated. Often in a few days the patient's condition changes from one of extreme debility to one bordering, in some cases, almost on euphoria. Pain is relieved, and this is one of the most gratifying results; the relief applies more particularly to pain due to metastases and is the more dramatic because it frequently occurs within a few days after orchiectomy.

The changes in the prostate are surprising. The characteristic stony, hard feel of the prostate to the examining finger is replaced by a softening and often by a reduction in size, although this does not always happen. When the patient has retention of urine this reduction of the size of the gland frequently results in a reestablishment of the urinary flow, but in a number of the reported cases endoscopic resection has been necessary. It is curious to note in this connexion that when relapses occur they often do so in the metastatic growths rather than in the prostate itself. Radiological examination of the metastases reveals regression, and in some cases bones which have been the site of extensive metastases return to normal, as far as can be discovered upon X-ray examination. Soft tissue metastases—for example, those of lungs and glands—also disappear.

It has been noted, too, that in these elderly men who are suffering from prostatic cancer castration produces none of the debilitating effects which occur in young men. They lose the libido certainly, but then of course they have less to lose.

Treatment.

Let me emphasize here again that the hormonal treatment of prostatic carcinoma is not curative. Current American opinion is that the treatment of carcinoma of the prostate, if the lesion is operable, should still be by radical perineal prostatectomy. (This operation is carried out in America more frequently as a routine measure than it is in this country.) Hormonal therapy is reserved for those cases in which operation is considered to be contraindicated.

Hormonal treatment may take the form of neutralizing the androgens by stilbœstrol, or of removing them by castration. To my mind, it is not logical to depend on neutralization of the androgens when one can remove them, at least in part, by a simple operation—that of orchiectomy—and the only indication for stilbœstrol therapy alone is in the treatment of those patients who are so ill that any operation is contraindicated.

The following routine of treatment is given as a pattern only, and like any other scheme of treatment, it may have to be modified in individual cases: (i) orchiectomy is performed; (ii) five milligrammes of stilbœstrol are given twice a day for seven days; (iii) five milligrammes of stilbœstrol are given once a day for seven days; (iv) a maintenance dose of one to three milligrammes per day of stilbœstrol is given for one to two months. This treatment is more intensive than is recommended by some authorities—in fact, a wide variation in dosage and methods exists. The acid phosphatase level of the blood should be checked at intervals, and this is the best guide as to the maintenance dose required after the first intensive course.

It may be asked: "Why not rely on orchiectomy alone, since by this means we cut off the supply of androgen?" The answer is that in many cases we do not remove all the androgen by this procedure. Then there are extragonadal sources of the androgen—the adrenals, for instance—which may produce it in such quantities that orchiectomy alone does not abolish production of all androgen. The rather large dosage of stilbœstrol following orchiectomy is advised to reinforce its effect, and this reinforcement is kept up by a smaller dosage for one to two months. How long it is continued will depend on one's observation of the patient. The level of the blood phosphatase is helpful in this connexion, and it is useful to have it estimated throughout the treatment. Obviously, if the patient has secondary growths in the bones, these should be examined radiologically.

Conclusion.

In conclusion, let me give you a brief description of a method of orchiectomy preferable to the guillotine operation. The skin of the scrotum is incised and the testis is exposed. An incision is now made through the *tunica vaginalis* and through the *tunica albuginea*. The substance of the testis bulges through the incision in the *tunica albuginea*, and is stripped away from it by gauze down to its pedicle. It is clamped and ligated. The coverings of the testis are approximated with a few catgut sutures and returned to the scrotum. The operation is simple, and what is left of the testis gives the patient the feeling that there is something there, and avoids that dreadful emptiness in the scrotum about which men always feel sensitive even in extreme old age.

References.

(1) C. Huggins and P. Clark: "Quantitative Studies in Prostatic Secretion", *The Journal of Experimental Medicine*, Volume LXXII, 1940, page 748.

(2) C. Huggins, W. W. Scott, and C. V. Hodges: "Studies in Prostatic Carcinoma", *The American Journal of Urology*, Volume XLII, November, 1941, page 997.

(3) C. P. Rhoads: "Newer Aspects of Cancer Research", *American Journal of Roentgenology and Radium Therapy*, Volume XLIX, Number 3, 1943, age 289.

(4) S. Murtis: "New Developments in the Treatment of Prostatic Carcinoma", United States Naval Medical Bulletin, Volume XLI, Number 4, July, 1943, page 1022.

(5) R. Chute, A. T. Willets, and J. P. Gens: "Experience in the Treatment of Carcinoma of the Prostate with Stilbœstrol and with Castration by the Technique of Intracapsular Orchiectomy", *The Journal of Urology*, Volume XLVIII, Number 6, December, 1941, page 682.

THE RATIONAL TREATMENT OF BURNS.

By S. A. SEWELL, M.B., B.S., M.R.A.C.P.,
Surgeon Lieutenant-Commander, Royal Australian Naval Reserve.

IN war, as in peace, severe burns present a problem resulting in a considerable loss of life and in much pain, suffering and subsequent disability in the community. Many methods of treatment have been lauded to the skies, and bitter has been the controversy between the different schools of thought. In the rational treatment of burns the following main principles must be borne in mind: (i) Our duty is to save life. (ii) Our duty is to relieve pain and suffering. (iii) Our duty is to limit subsequent disability in so far as we are able. With these considerations in mind we must consider the means at our disposal and the exigencies of the particular case in hand.

Before we consider treatment in a rational fashion we must first have a clear understanding of the pathological

processes which are going on. What causes death from burns? It can be stated dogmatically that death results either from peripheral circulatory failure, the result of hæmoconcentration by loss of fluid into and from the tissues, or secondly (less commonly and at a later stage), from toxæmia and possibly pyæmia or septicæmia, all the result of secondary infection by microorganisms. The later complications, such as bronchopneumonia and peptic ulceration, are a separate problem which need not be considered here.

The problem we have to consider is, how do these patholoical states arise, and how can we prevent them or assist the body in its fight against disease and death?

When heat is applied to the skin to such an extent as to produce a burn, the cells first of the surface layers and later of the deeper layers become damaged. If the heat is sufficiently intense, protein is coagulated. This usually occurs in the surface layers, whilst when we examine the deeper layers we find that less severe damage is done. Soon after tissue damage, cell enzymes begin to act on the damaged tissue with resultant breaking down of the large protein particles into smaller molecules—even at times to electrolytes. Thus arises an enormous increase in the osmotic value of the damaged tissues and the intercellular spaces, and indeed the cells themselves become enormously distended with fluid. Cloudy swelling of cells and œdema of tissues thus develop.

Capillary permeability is also so much affected that much protein escapes from the blood vessels into the tissues. In burns the tendency for the superficial layers to be coagulated usually results in the collection of fluid in the deeper layers, and this causes the raising of the bleb or blister with which we are so familiar. The enormous outpouring of fluid from the blood stream may result in circulatory collapse and death, especially when the burns are extensive, because of hæmoconcentration and loss of blood volume.

The original intense reaction to a burn is simply a modified acute inflammatory reaction, and with the above changes goes a pronounced local vasodilatation which persists for some days. As the products of tissue damage are gradually carried away, the œdema slowly subsides, the dead tissue at the surface is separated from the living tissue, and healing takes place by granulation tissue. Once the slough has separated, the pathological condition is a large ulcer. Secondary infection may occur, and this may result in further necrosis of tissue; this is especially apt to be extensive because of the lowered resistance of the damaged tissues to bacterial toxins. Finally, when the leucocytic barriers have walled off the infection and the superimposed necrotic tissues have been discharged as pus, an ulcer remains which heals in the usual fashion.

If these pathological processes are kept in mind, the treatment of burns resolves itself into the following principles: (i) replacement of fluid and protein in the blood stream; (ii) limiting of excessive exudation of fluid and of œdema; (iii) prevention of infection; (iv) application of various means of assisting healing—the use of suitable dressings, the removal of slough, and skin grafting; (v) prevention of deformity from excessive contraction of scar tissue.

When a patient extensively burnt arrives in a place where he can be treated, the first procedure is to relieve pain; this is done by the use of morphine. Measures are then at once taken to treat circulatory collapse; this is done by intravenous infusion of blood plasma. The amount of the latter required may be estimated by the use of the hæmoglobinometer. A rise of 10% in the hæmoglobin level represents approximately a 10% hæmoconcentration and can be combated with one pint of plasma. As exudation of fluid will continue for several days, the hæmoglobin value must be carefully watched, and should be estimated and recorded every two hours. Fluid should be given by mouth in the form of normal saline solution to which glucose and fruit juice have been added, and this should be taken in copious quantities.

After the initial collapse has been treated, consideration must be given to what form of local treatment is to be carried out on the burnt area. It was at one time the practice to tan the surface of burns with some coagulant, such as tannic acid, silver nitrate or triple dye. The rationale of this treatment (which is quite at variance with surgical principles) was that the surface coagulation limited serous exudation and in this way prevented the most serious complication—circulatory collapse. However, when plasma is available for intravenous infusion, such methods of treatment become obsolete. The large tough crust formed on the surface by tanning agents (especially triple dye) is extremely uncomfortable and is not impervious to bacterial invasion; hence infection beneath it is all too common. This is not aided by the prevention of drainage. The separation of this hard, leathery crust from the underlying delicate granulations causes damage to the latter with secondary hæmorrhage and is followed by considerable scarring. Finally, it must be most categorically stated that the tanning of any burn must be regarded as almost criminal, except where facilities for intravenous infusion cannot be obtained.

The obvious line of treatment is to render the burnt surface surgically clean and apply over it a dressing which, while bland and non-adherent, prevents the entrance of microorganisms and allows free drainage. This procedure is carried out under general anæsthesia, and for the purpose "Pentothal Sodium" is most satisfactory. The surface is cleaned gently, care being taken to avoid bursting blisters and causing further damage to the injured and weakened tissues. This is done first by thorough washing with soap and sterile water, of which many gallons should be used. This area is then treated with ether or alcoholic soap, which in turn is removed with ether or alcohol, and finally the surface is dried. The use of antiseptics on the already damaged tissues is considered inadvisable, although many authorities believe "Dettol" to be harmless. If both sides of the body are burnt, one side is treated first and the patient is turned, being laid on a sterile sheet. The use of ether has been said by its excessive cooling to increase shock. There seems no evidence to favour this view—in fact, cooling of the part is more helpful than harmful, in that it delays and diminishes the severity of the inflammatory reaction.

The practice of opening blisters and clipping away damaged tissue can have no justification. The statement that the serum in the blister forms a good culture medium for microorganisms has been advanced to favour this procedure. If proper aseptic surgical treatment is carried out, invasion with microorganisms will not take place.

The dressing of choice is sterile "Vaseline" gauze. It must be stressed that the gauze should be thoroughly impregnated with paraffin. For ease in application I have found the most satisfactory form a loosely rolled four-inch gauze bandage thoroughly impregnated with "Vaseline" and autoclaved. This is applied thickly, and then a thick layer of sterile wool is applied, over which a firm bandage is put on, the purpose of this pressure bandage being to limit œdema and excessive fluid exudation.

The use of sulphonamides on the surface prior to application of the dressing does not seem indicated. The use of these by mouth is just as effective, and absorption can be adequately controlled. Further, a liberal application of sulphanilamide tends to affect the consistency of the "Vaseline", which is then apt to adhere to the burnt surface.

The use of sulphonamides or of penicillin in the prophylaxis of infection has much to commend it; but in my experience, when adequate cleaning is carried out and proper aseptic dressings are applied, secondary infection does not occur—and after all, why should it?

When should the dressing be changed? This question cannot be answered arbitrarily, but in general it may be stated that this should be done as infrequently as possible. When the dressing is changed, the patient is placed in a sterile hypertonic saline bath, four times normal saline solution being used at about 100° F. The dressings are cut down and allowed to soak off in the bath. The area is then inspected (gown, cap and mask being worn), and loose sloughs are gently removed with scissors and forceps. The new dressing is applied as on the first occasion, and the patient is returned to bed, much more comfortable.

By the tenth day healing is usually well advanced and all sloughs should have become separated. The dressing is then removed, and it will be seen that most areas are healed, with the exception of areas of third degree burns. These will be granulating and should be skin grafted forthwith, small pinch grafts being used. The dressing is then reapplied, and generally only unhealed areas need be covered.

If this method of treatment is used, the most severe burn should be healed in twenty-one days, unless infection supervenes. However much care is taken, infection will sometimes occur. This is often due to streptococci exhaled onto the burnt area by the medical officer or his assistant. The importance of masks cannot be over-stressed. Infection should be treated *secundum artem*, according to the nature of the infecting agent. The sulphonamides or penicillin should be exhibited as indicated.

Restoration of function of all moving joints should be begun as soon as possible, and the patient should be urged whilst in the saline bath to put all joints through a full range of movements.

When burns are treated in this way, it can be anticipated in the majority of cases that healing will be complete within four weeks. In the case of localized burns the same principles of treatment apply; but here the danger from fluid loss is no longer a factor to be considered. The absorption of sulphonamides from the area will not reach toxic proportions, and hence the local use of sulphanilamide powder is indicated. It must, however, be remembered that when this is used, a thicker layer of "Vaseline" is required; even then there is some tendency for the dressing to adhere.

Conclusion.

In conclusion, it must be stated that each case of burns must be treated as an individual problem, and occasional modifications in treatment and technique will be necessary. The use of correct aseptic surgical technique is impossible without a well-trained team, and meticulous attention to detail is absolutely essential.

Acknowledgements.

I desire to thank the Director of Naval Medical Services for permission to publish this article, and I wish to express my indebtedness to the sick berth staff of the Royal Australian Navy for their capable help. The absence of any reference to the literature was unavoidable, as this article was written at sea without access to library facilities.

Reports of Cases.

A REPORT ON TWO CASES OF RUPTURED URETHRA.

By ROBERT S. LAWSON, M.S., F.R.C.S., F.R.A.C.S.,
Major, Australian Army Medical Corps.

(From an Australian General Hospital.)

CASES of ruptured urethra usually present a difficult problem in treatment, and different authorities have expressed widely varying opinions as to the best means of dealing with the condition. The subject was discussed at a meeting of the Section of Surgery of the Australasian Medical Congress (British Medical Association) in Adelaide in 1937, when, after several speakers had given their views, the chairman, Dr. G. Grey Turner, was moved to declare that he "entirely disagreed with practically everything that had been said" up to that point.[1] As the methods of treatment are thus apparently a matter of controversy, the report of two cases in which a successful result was obtained may be of interest.

Case I.

Private H., aged twenty-one years, was admitted to this hospital on August 14, 1943, at 2.30 p.m., having been buried by a fall of earth at a quarry half an hour before. He was suffering severely from shock on his admission to hospital and no precise diagnosis of his injuries could be made when he was first examined. Swelling and tenderness over the right pubis suggested fractured pelvis; but the whole abdomen was rigid and some intraabdominal rupture was suspected. Multiple abrasions and a Colles's fracture of the right wrist were also present. Morphine was given. Six hours later the rigidity had disappeared, but the suprapubic tenderness and swelling were more pronounced. There was very marked tenderness at the apex of the prostate on rectal examination, and when a catheter was passed only a few drops of blood were obtained.

A diagnosis of ruptured urethra was made and operation was undertaken eight hours after the accident. Under ether anæsthesia, the bladder was exposed by a mid-line suprapubic incision. There was much bruising around the bladder, but clear urine was found when it was opened. A hand was then passed into the cave of Retzius, the parts having been widely opened by the pelvic fracture. A rupture of the urethra was discovered below the apex of the prostate, with complete separation, so that the fingers could be passed right around the prostatic apex. Metal sounds were passed along the penile portion of the urethra, and from the opened bladder above, and a length of rubber tubing ("transfusion tubing") about one and a half inches long was manipulated over the ends of each of them. The sounds thus connected were then held together at their tips, and the lower sound was by this means pulled into the bladder. This manipulation is by no means so simple as certain facile descriptions may lead one to believe, the ends of the sounds being most difficult of access. Only the wide separation of the *symphysis pubis* from the fracture made it possible at all.

As the sound thus traversed the urethra, a number 12 Jacques rubber catheter was attached to its tip and pulled back along the length of the urethra, about three-quarters of an inch of its length being left in the bladder. It was secured by a long silkworm gut suture passed through the eye of the catheter, the ends of the suture coming out through the bladder to be "anchored" on the outside skin. The bladder was then closed around a large cystostomy drain and the wound was closed with a further drain in the cave of Retzius. The bladder was thus drained by urethral catheter and suprapubic drain tube, both later connected by tubing to bottles at the side of the bed. The Colles's fracture of the left wrist was reduced.

The patient was suffering considerably from shock after operation, and a transfusion of 700 cubic centimetres of blood was given. In the following week, though gravely ill, his condition improved steadily. Thirty grammes of sulphanilamide were given by mouth during the first five days. X-ray examination revealed dislocation inwards of the distal two-thirds of the right half of the pelvis with oblique fracture through the ilium below the sacro-iliac joint, separation of the *symphysis pubis*, displacement downwards and outwards of the left half of the pelvis and fracture of the inferior ramus of the left pubis. However, no special measures were undertaken to deal with this fracture except for the placing of a binder over the wound dressings, which perhaps helped to hold the pelvis together.

The arrangement of the bladder drainage was left undisturbed for fifteen days. The suprapubic tube was then removed, as nearly all the urine was draining by urethral catheter. Two days later the urethral catheter was also removed and the patient began passing urine without any special difficulty. By the twenty-fourth day all urine was being passed *per urethram* and the suprapubic wound was dry. However, the patient commenced to have a "swinging" temperature. A further course of chemotherapy (thirty grammes of sulphathiazole in five days) was given without much effect. Whether this fever was from an ascending urinary infection or from pelvic cellulitis could not be determined; the appearances in an excretion pyelogram were normal.

On the forty-first day, under "Pentothal" anæsthesia, metal sounds were passed along the urethra. Much difficulty was experienced in passing the first sound owing to a dip in the course of the urethra at the point of rupture. When this was recognized further sounds were easily passed up to the largest size (number 13/16). A rubber catheter was then tied in for twenty-four hours and a third course of chemotherapy was given (thirty grammes of sulphathiazole). The patient passed urine again without difficulty after the removal of the catheter. The temperature also settled down.

At the end of seven weeks the patient was sitting out of bed. The suprapubic wound was healed except for a small sinus over the *symphysis pubis*. His micturition was to all intents normal in character and frequency. His only complaint was of neuralgic pain in the sole of the right foot—apparently causalgia of the right sciatic nerve. At this stage he was transferred out of our care to his own State.

Four months after his accident, the patient was shown at a clinical meeting in another State by Major M. S. Alexander.[2] He was then walking about with ease. Several small sequestra had been removed from the suprapubic sinus. Sounds had been passed periodically without difficulty, and the appearances in a urethrogram were normal. After healing and discharging intermittently, the suprapubic sinus finally healed just six months after the accident. The last available report of this patient is dated May 22, 1944, over nine months from the date of operation. He was then passing a good stream of clear urine and having no trouble with micturition. All movements at the hip joints were free. His general condition was stated to be "very good".

Case II.

Private E., aged twenty-four years, was admitted to this hospital on August 29, 1943. He had been involved in a motor-car accident the previous night and was taken to a field ambulance, where a superficial laceration of his left knee was excised under ether anæsthesia. The next day the patient was discovered to have blood on the end of his penis; he was unable to pass urine, and had not done so since the accident. He was therefore transferred to this hospital.

His general condition was fair on his admission to hospital. Slight bruising of the posterior part of the perineum was present, and pain was elicited on attempted compression of the iliac crests, suggesting a fractured pelvis. The bladder was not distended; but in tropical climates a longer period of retention than eighteen hours is required to produce distension. A rubber catheter could not be passed into the bladder, and only a few drops of blood were obtained on attempted catheterization. A diagnosis of ruptured urethra was made and operation was undertaken, twenty hours after the accident.

Under ether anæsthesia the bladder was exposed by suprapubic mid-line incision. It was found to be intact, though bruised around the base. Clear urine was obtained when it was opened. In contrast to the previous case, the anterior attachment of the bladder to the *symphysis pubis* had not been disrupted; that is, there was no separation of the symphysis nor opening up of the cave of Retzius, and the site of rupture was therefore not apparent. Rather than carry out a wide exploratory dissection from above to discover the rupture, we placed the patient in the lithotomy position and a mid-line perineal section was made. A complete rupture of the urethra was exposed, high up and apparently at or close to the membranous portion. There was a wide separation of the ruptured ends (about one inch or more). A partial approximation of the "roof" of the urethra was performed with difficulty, the proximal segment being very high up and almost inaccessible. Number 1 chromicized catgut sutures were used.

A number 12 Jacques rubber catheter was then passed into the bladder from the urethral meatus and across the line of sutures. It was secured by a silkworm gut suture through its tip in the bladder as before. The bladder was then closed around a cystostomy drainage tube, and a drain was also placed in the cave of Retzius. The perineal wound was left widely open, the rubber catheter being exposed in its depth and covered only by the wound dressings. A transfusion of 600 cubic centimetres of blood was given.

The patient's condition after operation was satisfactory and he made an uninterrupted recovery. A course of sulphathiazole treatment was started on the day following operation, thirty grammes being given in five days. X-ray examination revealed a fracture of the superior and inferior rami of the left pubis with comminution of the inferior ramus, and a probable fracture of the left ischium in the region of the acetabulum. No special measures were undertaken at any stage for the treatment of these fractures.

The suprapubic drainage tube was removed on the eighteenth day and the catheter two days later. There was no evidence of urethritis or other ill effect during this period. Three days after removal of the catheter the patient was passing nearly all urine *per meatum* without difficulty and the perineal wound was almost healed. On the thirty-second day metal sounds were passed under "Pentothal" anæsthesia. The urethra appeared to run a normal course and sounds were passed up to the largest size (number 13/16) without difficulty. No reaction followed this procedure.

At the end of five weeks both the perineal and suprapubic wounds were healed. The patient was passing clear urine without pain or difficulty and with normal frequency. The general condition was satisfactory, and the patient began sitting out of bed. At this stage he was transferred to his own State.

Sounds were passed again on December 3, 1943, and he was then reported to have been "passing urine freely and without any difficulty". He was returned to duty as a B class man a little over three months from the date of operation. Periodical passage of urethral sounds is to be carried out.

The last report I have of this patient is dated July 6, 1944, over ten months from the date of his accident. He was then in good health, working full time as a clerk in a base unit. He was free from any evidence of stricture and had no urinary symptoms. He stated that he felt quite well except for an ache in his pelvis during cold weather.

Discussion.

The experience of these cases (together with recollections of previous failures) prompts me to suggest the following considerations in regard to intrapelvic rupture of the urethra.

1. The diagnosis can easily be missed, as in the second case, if this possibility is not kept in mind. Examination of the perineum is frequently overlooked in the general examination of a seriously injured patient. It should never be omitted, particularly when there is a possibility of crushing injury—for example, in motor-car accidents; a tell-tale bruising is the first key to the diagnosis. Rectal examination may also be a helpful diagnostic measure, though it is not usually mentioned in this connexion. It can be performed with little disturbance, with the patient in the dorsal position as he lies in bed.

2. The passage of a catheter for diagnosis is of value and does no harm. This and the remaining points to be mentioned have all been matters of dispute.[1]

3. Suprapubic cystostomy is the essential first step in operative treatment. When the patient is severely shocked and suffering from multiple injuries, this may be the only measure which is feasible. To attempt more in such a case may be to kill the patient.

4. Manipulation of a catheter along the urethra by means of sounds as described is difficult, and it may not be possible unless the *symphysis pubis* is widely separated by the pelvic fracture. Perineal section would then seem to be preferable if the patient's general condition will stand it.

5. An indwelling catheter after operation is a valuable means of treatment in either method; it is well tolerated, acts as an effective splint and has no serious ill effects.

Acknowledgement.

This article is published with the permission of the Director-General of Medical Services.

References.

(1) "Traumatic Rupture of the Urethra and its Treatment", THE MEDICAL JOURNAL OF AUSTRALIA, Volume II, October 23, 1937, page 720.

(2) THE MEDICAL JOURNAL OF AUSTRALIA, Volume I, April 1, 1944, page 305.

Reviews.

AVIATION MEDICINE.

THE first edition of "The Principles and Practice of Aviation Medicine", by Harry G. Armstrong, Colonel, Medical Corps, United States Army, was reviewed in these columns in June, 1940, and the opinion was expressed that the book would take its place as a standard treatise on the subject. That this surmise was correct is proved by the favourable reception bestowed in the United States of America and Britain and by the growing demand for a new edition. This has now appeared and will assuredly be given a warm welcome, for it embodies many improvements on its predecessor, excellent though this was.[1]

[1] "Principles and Practice of Aviation Medicine", by Harry G. Armstrong, M.D., F.A.C.P.; Second Edition; 1943. London: Baillière, Tindall and Cox. 9" × 6", pp. 524, with illustrations. Price: 36s.

The book covers a wide field and deals with every aspect of aviation from a medical standpoint. Chapter I is historical; Chapter II gives the author's views on the qualifications of the flight surgeon, and it is interesting to note that an ability to fly is considered valuable if not essential. Chapters III and IX give in detail the technical procedures for the examination of intending pilots. It is pointed out that in the last war the major activity of the flight surgeon was to make good selections by appropriate tests, whereas now the care of the flier is rightly regarded as of equal or even greater importance. In the remaining chapters the actions of flying conditions, including changes in altitude, acceleration and temperature, on the various organs and on the mentality of the pilot are dealt with and admirable accounts are given of air-sickness and emotional reactions and the means to combat these. Especially valuable is the section on false sensations in flight and the dangers associated with them. A broad and wholesome sanity is obvious throughout the book. Thus the author reprimands those medical officers who use their authority to threaten pilots with "grounding" because some punctilio of ordered exercise has not been carried out; also the type who "looks upon his charges either as infants or criminals"; again a special rap on the knuckles is given to those "who act in the capacity of walking psycho-analysts. These individuals are usually those poorly trained in psychology with only sufficient knowledge of the specialty to make them a nuisance". This is most refreshing to read, and it is to be hoped that the warning will be taken to heart throughout the wide circles in which this work will be used as a standard text-book.

A few minor criticisms, in no way reflecting on the general merit of the book, may be permitted. The section dealing with sanitation and quarantine could be extended with benefit. The description of the physiology of free fall is based on the author's own investigations and is correct enough, but the brilliant work of his countrymen Ivy and his collaborators has not been used. That the body fluids would boil at an altitude of 60,000 feet may be true, but this is an academic consideration, for human life cannot exist above 40,000 feet unless in a closed cabin, and should this burst the mere boiling would not matter much, for death would be swift anyhow. There is no mention of the increased ventilation of the antra and sinuses and the danger of infected mucus being blown into these cavities during a rapid dive or a parachute fall. The formula for the decomposition of radium on page 184 should be amended. The only criticism of a serious nature which we would advance is that the procedures for the examination of the eye are far beyond the capacity of any but trained ophthalmologists. The flight surgeon must not only go through the usual discipline of medical study, but he should, in this author's opinion, be able to fly or at least have a wide personal experience of flight conditions. Surely it is too much to ask that he use correctly the phorometer trial frame with multiple Maddox rods and rotary prisms, the tangent curtain and the stereo-orthopter. Even the simplest examination of the fundus with the ophthalmoscope would be better if left in the hands of the specialist. Having entered this protest, we should like to end in a note of warm praise and congratulation for a fine work.

MEDICAL BACTERIOLOGY.

IT is unwise nowadays to attempt to crowd too much information into a very small book. Accuracy is inevitably sacrificed to brevity, and the whole volume is bound to remind one a little of the "Digest" type of periodical. A digest is an unsatisfactory sort of meal; you may be able to swallow it quickly, but it has many disadvantages.

"Medical Bacteriology", by L. E. H. Whitby, is a small handy volume, designed (to quote the preface to the first edition) "to present in brief form the accepted views on the relation of bacteria to medicine".[1] The first part contains descriptions of the common pathogenic organisms, and includes some elementary protozoology and helminthology as well as a chapter on fungi and a chapter on viruses. The second part of the book, entitled "Applied Bacteriology", includes chapters on chemotherapy, on the bacteriology of water, milk and food, and on laboratory aids in the diagnosis and treatment of individual diseases. The outlines of treatment are of necessity inadequate and might well, one would think, have been omitted. There is no mention of chemotherapy in the treatment of anthrax, and surely it is out of place to attempt to describe the treatment of asthma in a book such as this. It is true, as the author states in his preface to the present edition, that a book of this size must of necessity be somewhat dogmatic, but it is important for a writer so eminent as Whitby to avoid statements of doubtful accuracy. The assertion that "syringes may be kept sterile by storage in absolute alcohol" is open to question, and many will not agree with the author's views on the preparation and use of vaccines or on bacteriophage.

These, however, are minor defects in a book which contains much essential information in a small space. It should prove very useful to the busy general practitioner or to the medical student for whom it is primarily intended and who will find in it many practical and useful suggestions. The text is pleasingly varied by 81 rather diagrammatic illustrations and 13 tables; and the print is clear and good.

[1] "Medical Bacteriology: Descriptive and Applied, including Elementary Protozoology and Helminthology", by L. E. H. Whitby, C.V.O., M.A., M.D. (Cambridge), F.R.C.P. (London), D.P.H.; Fourth Edition; 1944. London: J. and A. Churchill, Limited. 8" × 5¼", pp. 351, with many illustrations. Price: 14s.

AFTER-TREATMENT.

THE fact that "After-Treatment", by H. J. B. Atkins, has already within two years called for a second edition is sufficient proof of its excellence and of the demand for such a detailed exposition of the care of patients following operation.[1]

This edition presents a new chapter on the post-operative treatment of children which should prove very helpful. It presents very full details for the feeding of small patients following operation for pyloric stenosis and covers also the question of plastic operations for congenital malformations of the face. There are new sections on post-operative coronary thrombosis and on the management of diabetic patients. The chapter on rehabilitation is very timely, and the very complete details of remedial exercises and occupational therapy should prove of great value to all practitioners in the after-war period.

HISTOLOGY FOR MEDICAL STUDENTS.

THE third edition of "A Textbook of Histology for Medical Students", by Evelyn Hewer, reflects the author's long teaching experience in its concise and clear presentation of the subject.[2] Recent developments in the art of photomicrography in colour, together with the more vital outlook on the subject of histology, have greatly enlarged the scope of modern text-books on the subject. The use of tissue cultures, intravital injections and even direct microscopic observation of living tissues *in situ*, have given new conceptions which must still be tempered, however, by the difficulty of obtaining sources of fresh human material. Most books encompassing all these aspects are too large and detailed for general use by medical students and are essentially books of reference.

Dr. Hewer's book provides an accurate account of all the essential details of normal tissue structure and makes no attempt to discuss academic and controversial points. The primary tissues are described with admirable clarity and the relation of structural change with function is emphasized where possible. The chapters on connective tissue, peripheral vascular system, meninges and serous membranes are first rate. The book is eminently suitable as an introduction to histology for students when used in conjunction with the larger text-books for reference.

This edition contains additional illustrations, though it is a pity that the photomicrographs do not comprise a greater proportion of human material. The large number of simple drawings and diagrams is particularly useful in a teaching book, since they provide the student with considerable aid in interpreting his own slides as well as the photomicrographs in the text.

[1] "After-Treatment: A Guide to General-Practitioners, House-Officers, Ward-Sisters and Dressers in the Care of Patients after Operation", by H. J. B. Atkins, D.M., M.Ch. (Oxon.), F.R.C.S. (England); Second Edition; 1944. London and Melbourne: Macmillan and Company Limited. 8¾" × 5½", pp. 325, with 60 illustrations. Price: 18s. net.

[2] "Textbook of Histology for Medical Students", by Evelyn E. Hewer, D.Sc. (London); Third Edition; 1944. London: William Heinemann Medical Books Limited. 9¼" × 6¾", pp. 371, with many illustrations. Price: 17s. 6d. net.

The Medical Journal of Australia

SATURDAY, DECEMBER 2, 1944.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

PENICILLIN IN THE TREATMENT OF SYPHILIS.

THE discovery that penicillin had an extremely powerful effect in certain bacterial infections was naturally followed by investigations into its possible use in other conditions. The Committee on Chemotherapeutic and Other Agents of the Division of Medical Sciences of the National Research Council of the United States, acting for the Committee on Medical Research of the Office of Scientific Research and Development, instigated an inquiry into the treatment of early syphilis by penicillin, and a preliminary report of the study was published at the end of 1943 by J. F. Mahoney, R. C. Arnold and Ad Harris.[1] These workers first of all found by experimenting with rabbits that penicillin had some spirochæticidal activity and then treated with nothing but penicillin four patients who were suffering from primary syphilis. This early application of the test to man was justified "by the general nontoxic character of the drug and by the knowledge that observations as to early effectiveness could be carried out without placing in jeopardy the patient's chance for ultimate recovery in event it became expedient to resort to conventional arsenic therapy". The immediate results of the treatment of these four patients were very striking—spirochætes disappeared from the primary lesions by the sixteenth hour after the start of treatment, the lesions healed and positive serological findings were reversed. (The treatment consisted of an intramuscular injection of 25,000 units of the drug at four hour intervals night and day for eight days. In all 48 injections were given and the total amount of the drug was 1,200,000 units.) As a result of these observations and of other experimental studies (so far unpublished) a cooperative study was organized early in September, 1943, and was carried out under the specific direction of the Subcommittee on Venereal Diseases of the National Research Council. A Penicillin Panel was appointed by this subcommittee and members of this panel with others have prepared papers[1] which were presented to the Section on Dermatology and Syphilology at the annual meeting of the American Medical Association in June, 1944. These papers are of such far-reaching significance that they must be brought to the notice of Australian practitioners.

The first paper in this series reports an extension of the original investigation of Mahoney, Arnold and Harris, and is presented by them together with B. L. Sterner and M. R. Zwally. Three of the four patients first treated remained "clinically and serologically negative" for periods up to eleven months. The fourth patient was classed as a failure, because after 286 days strongly positive reactions were given to serological tests; a single ulcerative lesion on an indurated base was found on the inner surface of the lower lip (the original lesion had been on the penis), and it was thought probable that reinfection was responsible. The study was continued and approximately 100 patients have been treated. Owing to the rapid disappearance of lesions, the main reliance in the evaluation of treatment has been placed upon serological tests, and in order that control might be as complete as possible, seven accredited methods were used. On the basis of an arbitrary minimum of seventy-five days of satisfactory observation after treatment, the records of 52 patients were available for scrutiny. The average duration of observation was 135 days. Thirty of the 52 patients had "dark field positive primary syphilis". Twenty-five of the thirty became "clinically and serologically negative". Of the remaining five, two could not be classified, but were likely to be classed in the satisfactory group; one developed a clinical relapse nine months after treatment (this was the patient possibly reinfected); one had a serological relapse after an initial favourable serological trend of 112 days after treatment; one had a clinical relapse after 84 days of practically unchanged high titre positive serological reactions. Of the 22 patients who displayed evidence of secondary syphilis and who were well into the serologically positive stage of the disease at the time of treatment, eleven progressed to "seronegativity" or had displayed a consistently satisfactory trend in that direction. Four patients showed a distinct tendency towards a recurrence of high titre reactions and had therefore to be classed among the serological relapses or failures. Two additional patients were looked on as probably classifiable among the failures and five were displaying a serological trend presaging an unfavourable outcome. In commenting on these results, the authors point out that very early infections respond in the most favourable way and that the increase in probable failures among patients with secondary syphilis indicates the need for a more vigorous therapy than has been used in their study. They also draw attention to the fact that in the arsenic therapy of syphilis and the sulphonamide therapy of gonorrhœa a certain proportion of persons fail to show the same curative response as the majority of other persons; they add that a similar characteristic seems to be emerging in the penicillin therapy of syphilis.

Having set out a few of the details from the preliminary reports of Mahoney and his collaborators, we may now turn to the other contributions. The first is a preliminary report on the treatment of 1,418 patients suffering from

[1] *Venereal Disease Information*, December, 1943.

[1] *The Journal of the American Medical Association*, September 9, 1944.

early syphilis, and this report emanates from members of the Penicillin Panel already mentioned—J. E. Moore, J. F. Mahoney, W. Schwartz, T. Sternberg and W. B. Wood. That this report is also preliminary is shown by the fact that of the 1,418 patients, 671 had been followed up for only one to four weeks and 307 for periods of from five to eight weeks; six had been followed for periods of from 25 to 48 weeks; only 113 had been followed for four months or longer. When therefore it is stated that the results were satisfactory in 95·8% of cases, this period of brief observation must be borne in mind. Some interesting observations were made. Confirmation was obtained of the profound immediate effect of penicillin in early syphilis in regard to (*a*) disappearance of surface organisms from open lesions, (*b*) healing of lesions, (*c*) a trend towards reversal of positive serological findings. At the same time these immediate effects were in general identical whether the dosage was 60,000 or 1,200,000 units or any figure between these two when the drug was given by the intramuscular route every three hours day and night to a total of sixty injections in seven and a half days. The same intermediate effects were apparent within the dosage range of 300,000 to 1,200,000 units given by the intramuscular route every three hours day and night to a total of thirty injections in four days. The optimum time-dose relationship could not be determined by these findings; for this purpose the incidence of relapse had to be used. The incidence of relapse in patients treated by the intramuscular route was found to be in direct proportion to the total dosage—nearly 30% when 60,000 units were given and 2% with 1,200,000 units. Relapse for some unaccountable reason seemed to be more frequent after intravenous than after intramuscular administration. A direct relationship was found between the stage of the disease at which treatment was started and the incidence of relapse—3·2% for "seronegative primary" syphilis, 5·0% for "seropositive primary" syphilis and nearly 10% for early secondary syphilis. The lowest incidence of relapse, as well as the most favourable serological response, was noted in small groups of patients who were treated with 60,000 and 300,000 units of penicillin respectively together with a known subcurative dose of "Mapharsen". It should be mentioned that one group of patients who received 300,000 units of penicillin *plus* 320 milligrammes of "Mapharsen" showed initial results that were as good as those shown by patients receiving four times as much penicillin without "Mapharsen".

Yet another communication deals with the action of penicillin in late syphilis and is called a preliminary report; the authors are J. H. Stokes, T. H. Sternberg, W. H. Schwartz, J. F. Mahoney, J. E. Moore and W. B. Wood. Their observations are based on material collected in the observation of 182 patients for periods ranging from eight to 214 days after the institution of treatment. The paper is full of interesting detail which cannot be described at present. It must suffice to quote the general statement with which the authors open their discussion. They write:

> Penicillin has distinctly beneficial serologic and clinical effects on neurosyphilis, including early and late manifestations, not excepting tabes and paresis, and including asymptomatic neurosyphilis. Its action on gummatous manifestations of skin mucosæ and bones is so striking and complete that it seems unnecessary to collect further cases merely to demonstrate it as such. In ocular syphilis, simple inflammatory processes respond; later and more complicated lesions such as the optic neuritides and interstitial keratitis recover, relapse, present resistance and residues proportional to damage already done. This statement is probably true of visceral syphilis and of special localized processes and eighth nerve involvement.

This statement, it must be emphasized, cannot be taken at its face value; it is, as the authors insist, sharply limited by qualifications involving the duration of the period of observation and small numbers in individual sections of the work, and by wide variation in time-dosage relationships and little uniformity as to the time and type of testing and of procedures of rechecking. This plea for caution is one that must be made for all this work on penicillin and syphilis. It looks as though we had suddenly drawn near to a promised land replete with wonders of which we have dreamed; possibly we have, but before we essay to enter we must be sure of the ground under our feet and we must not expect too much of the wonderful weapons of therapeusis that we see before us. Undue haste may involve us in difficulties, making us deficient in the help that we would give, if not hurtful, casting a slur on the science that we preach, and making us bunglers of the art that we claim to practise. This work is branded all through as preliminary, and it must be treated as nothing more. The clinical observations and little else have been recorded; we have no account of the early experimental work on rabbits or of any other experimental laboratory investigations. These reports are an invitation to workers in other parts of the world to undertake investigations that will add to knowledge on the subject, for penicillin is not yet ready for mass application in syphilis. J. E. Moore, in closing the discussion when the reports were presented, spoke of a note of restrained optimism. He said that our attitude should be one of hopefulness, but insisted that we needed to realize that we were still in the process of learning how to use the drug. If clinicians keep these considerations before them they will take no false step.

Current Comment.

TREATMENT BY ALKALIES IN BLACKWATER FEVER.

PRACTICAL acquaintance with blackwater fever in tropical war zones has not only turned the attention of many medical officers in the services to the intensive administration of alkalies in this often serious emergency, but also to the treatment of other conditions in which hæmolysis may occur. B. G. Macgraith and R. E. Havard have published a paper which directs criticism at high alkali dosage in blackwater fever.[1] They disagree with the argument that the suppression of urine, which is the chief risk of this condition, is due to a blocking of renal tubules by derivatives of hæmoglobin. They point out that the work of Baker and Dodds showed that acid hæmatin is most readily precipitated *in vitro* when there is a concentration of sodium chloride of at least 1% with an acid medium. To these conditions must be added the fair assumption that the number of tubules blocked must be great. Macgraith and Havard suggest that the number of blocked tubules must approach 100%, though this can only be an assumption. However, these authors are on surer ground when they demonstrate that at the onset of anuria the urine is alkaline as often as it is acid. They also quote Ross, who showed that 1% concentration of salt was not attained in the urine immediately before suppression occurred. Further, autopsy does not always confirm extensive tubular blocking. It is known, too, that

[1] *The Lancet*, September 9, 1944.

where the excretory function of the kidney is impaired, as it is in blackwater fever, the urine may remain acid, even in the presence of severe alkalosis. Macgraith and Havard therefore join issue with authorities who direct that sufficient alkali be given to keep the urine alkaline, pointing out that the reaction of the urine is not necessarily an index of the amount of alkali which should be given. They quote results obtained by them in West Africa in the treatment of patients given intensive alkali treatment, and show that alkalization of the urine did not prevent anuria, and that in about half the cases this treatment did not succeed in producing an alkaline urine. It must, however, be admitted that this is not quite convincing, as the blow falls so swiftly in blackwater fever that damage may be done very early, perhaps too early for subsequent treatment, however heroic, to succeed. But it must be conceded that alkalosis is not a trifling risk. It is easier to produce where renal damage exists and of itself tends to increase existing renal damage. Clinicians are familiar with a number of instances of this risk in all manner of conditions in which alkalies in large doses are used. Solutions of sodium lactate found useful in diabetic coma have been used extensively in these hæmolytic crises, and are free from some of the objections to certain other alkalies like bicarbonate. But whatever alkali is used, it can be used to excess.

Macgraith and Havard lay stress on the damage to tubular epithelium in blackwater fever, and remark that patients recovering from oliguria or anuria do not always pass quantities of debris and pigment, but pass abundant clear urine in some cases, and show delay in regaining full renal function. This is not at all unexpected. The final argument used by these workers against the intensive alkaline treatment is that it has failed to reduce the mortality. Actually it is hard to draw safe deductions from their tables, for blackwater fever is a disease whose severity depends on a number of factors. The authors of this article perhaps have been too sweeping in their disapproval of the intensive alkali treatment of blackwater fever, just as some of the advocates of the method have been too dogmatic and too optimistic. They have done a service in pointing out what a two-edged weapon alkali is. Their contention that the administration of alkali in blackwater fever should be controlled where possible by estimation of the alkali reserve is no doubt correct, but this ideal will be seldom attained. However, it would be wise for those employing rapid and intensive methods of alkali administration to remember that the treatment is itself not free of danger, and that the goal of an alkaline urine should not be blindly pursued without a realization of the physiological processes involved.

ANTITUBERCULOSIS WORK IN WESTERN AUSTRALIA.

In a recent review in these pages of the report of the Public Health Department of Western Australia all reference to the work carried out at Wooroloo Sanatorium was omitted because the work is of such importance that special attention should be drawn to it.

The report on the sanatorium's activities comes from the pen of Dr. Linley Henzell, who has held the office of medical superintendent since August, 1941. He divides his account of the work into two parts; the first deals with sanatorium treatment and the second with "case finding" and the after-care and supervision of patients after their discharge together with certain activities among contacts of the patients. That sanatorium treatment is the be-all and end-all of antituberculosis activity is an idea that is not so prevalent as it used to be, but as far as can be gathered there are still many people who hold the old-time view. This is one reason why means should be found of making public such documents as Dr. Henzell's report. There are usually in the sanatorium 230 patients and there is accommodation for 220. To minimize overcrowding approximately twenty civilian patients have been admitted to another institution, the Edward Millen Home. At Perth Hospital there are generally about fifteen patients receiving specialized surgical treatment. This has been necessary because Wooroloo has no proper operating theatre. In "the room used as a theatre" the only surgical procedures that can be undertaken at present are artificial pneumothorax inductions and injections for the production of pneumoperitoneum. The work carried on at the sanatorium has been increased since 1941 partly because there has been an increase in surgical treatment and partly because patients have been admitted from the services and from the Repatriation Department. The increase in the numbers of patients has meant an increase in the numbers of nurses. In August, 1941, the numbers of trained and untrained nurses were nine and 48 respectively; these numbers have risen to 11 and 57. It is estimated in England that in a sanatorium where full surgical treatment is carried out the proportion of patients to nurses should be in the ratio of 2·5 to 1. Although "full" surgical treatment is not carried out, the sanatorium is obviously understaffed. The number of applicants for training is steadily declining, and we can well understand that "if the position is not improved the shortage will become critical". We should imagine that considerable difficulty is being experienced.

Dr. Henzell has some interesting remarks to make about the renovation and modernization of the premises. Soon after he took up his duties proposals for urgent renovations and alterations were made and approval was given for the expenditure of the necessary money, but "war difficulties of labour and material have prevented much being done". However, a new X-ray plant has been installed and certain necessary electrically heated trollies and other apparatus have been acquired for the kitchen. The ward accommodation is poor and certain urgently needed additions are mentioned. "The wards are too widely dispersed for efficient nursing and quite unsuited for major surgical treatment." Plans are being made for post-war expansion. A treatment block containing a hundred beds, an operating theatre, and a "refill" room is projected, but further additions are required.

In the second part of his report Dr. Henzell first of all refers to case-finding and the work of tuberculosis clinics. A clinic is held at the Perth Hospital, and Dr. Henzell enjoys the cooperation of Dr. R. le P. Muecke, the medical superintendent; a clinic has been started at Fremantle Hospital and negotiations are in progress for the establishment of a clinic at Kalgoorlie. Dr. Henzell recommends the appointment of a whole-time tuberculosis medical officer for the metropolitan district of Perth. It is, however, on Dr. Henzell's efforts in occupational therapy and colonization that attention should be focused. He makes a short statement on the value of tuberculosis colonies such as Papworth and he has made a start to create something of the kind in Western Australia. It would have been very easy for him to sit back and recommend the Government to put money on the estimates for such a purpose. But he believes that "the Lord helps those who help themselves" and he has induced the patients and the staff of the sanatorium to raise money by various means towards capital to found a colony. Since April 1, 1942, the staff and the patients have raised no less a sum than £1,000. The result is that the State Government has given two sums totalling £1,750, and as a result of other efforts the total now stands at £4,250. Already a carpenter's shop and a tinsmith's shop are in working order; vegetable gardens and an orchard are in production. These ventures are successful and some products have been sold. Also a hostel is being built and is almost completed. A new house has been built at the farm for the farm manager, almost exclusively by labour from among the patients.

From this short description of the activities at Wooloroo it is clear that the work is being carried out with energy and imagination. When the State of Western Australia has become blessed in this way, it must see that Dr. Henzell obtains all the help and encouragement that he needs. He has shown the government authorities how money should be spent and also that he is not content to do nothing while government decisions are being made.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Tyrothricin in the Treatment of Marginal Corneal Ulcers.

S. BLOOMFIELD (*American Journal of Ophthalmology*, May, 1944) has used tyrothricin in the treatment of marginal ulcers of the cornea due to Gram-positive organisms, which had proved resistant to treatment by ordinary measures. An alcoholic solution of tyrothricin was suspended in distilled water in a concentration of 0·2 milligramme per cubic centimetre. An ointment was also made, consisting of tyrothricin in a petrolatum-lanolin base, in the same concentration (1:5,000). Experimental work on rabbits and on human volunteers proved that these preparations were innocuous when instilled into the eyes. No local or systemic toxic reaction has followed their therapeutic application. The author reports four cases in which tyrothricin was used with gratifying results. He points out that the ætiology of primary superficial ulcerations of the corneal margin is unknown, but states that, whatever the cause, it seems probable that infection, either primary or secondary, may be a factor in the persistence of the lesion, and one against which active treatment is indicated. When the more easily available antiseptics prove futile, tyrothricin seems to be an effective therapeutic agent. Studies are proceeding to determine its effectiveness in other diseases of the eye. Further trial will be necessary to confirm the favourable impression created by this new, safe and effective antibacterial agent.

Meningococcal Conjunctivitis.

F. H. THEODORE AND P. F. KOST (*Archives of Ophthalmology*, March, 1944) describe eight cases of meningococcal conjunctivitis, in which the diagnosis was made only because it was the routine policy to study smears of secretions stained by the Gram method in all cases of acute catarrhal conjunctivitis. They point out that the incidence of extrameningeal infections increases at times when meningococcal meningitis is prevalent. Apparently the conjunctiva is a common site of extrameningeal involvement. The importance of the recognition of this type of conjunctivitis is twofold: first, it may be the first stage of meningococcal meningitis, and secondly, even if the process remains localized to the eyes and is cured by non-specific routine measures, the patient may become a carrier of the organisms.

A. B. MANGIARACINE AND A. POLLEN (*ibidem*, April, 1944) report ten cases of acute suppurative conjunctivitis of meningococcal origin occurring within a period of five months. In none of them so far as could be determined was there a definite history of exposure or of general prodromal symptoms. Five of the patients were stated to have had a "cold" at some time prior to, or at the time of, the onset of the ocular infection; but this appeared to bear no particular relationship either to the onset or to the course of the ocular symptoms. The ages of the patients varied from fourteen weeks to fifteen years; all the patients were males. Of the ten cases, frank meningitis (type I) developed in one and meningococcal septicæmia (type I) with abortive meningitis in another. Culture of material from the eyes yielded type I meningococci in four other cases and type II meningococci in two cases. In the first two cases the organism was not typed. In six cases both eyes were involved and in four cases one eye only was affected. The cornea was involved in five cases; superficial ulcers developed in two cases and corneal œdema alone in three cases. In no case did permanent residual ocular change follow therapy. Treatment consisted of local and oral chemotherapy in five instances, of local chemotherapy alone in four instances and of irrigations with zinc sulphate alone in one instance. Oral chemotherapy was employed only in cases in which corneal involvement or systemic or meningeal symptoms were present. Neither the degree nor the course of the ocular infection seemed to be modified by the addition of oral treatment with sulphadiazine, and the patient who received zinc sulphate alone did as well as the rest. With the exception of the patients who had meningeal involvement, the average length of stay in hospital was eight days; the ocular discharge subsided in three to five days, and the eyes became white and the process quiescent in seven days. The authors state that the apparent recent increase in the incidence of suppurative meningococcal conjunctivitis, which was previously considered rare, leads to the belief that earlier infections may have been missed because of the morphological resemblance of the organisms to those in the Neisserian group. The discovery of Gram-negative, intracellular diplococci in a smear from the conjunctiva of a patient suffering from acute suppurative conjunctivitis usually arouses suspicion of a gonorrhœal infection. Differentiation by cultural methods determines the diagnosis.

Simple Glaucoma.

O. LOWENSTEIN AND M. J. SCHOENBERG (*Archives of Ophthalmology*, May, 1944) discuss the origin and significance of the nervous factor in simple glaucoma. They state that in all cases of primary simple glaucoma studied, constant characteristics of the pupillary reflex to light were shown by both eyes. In the initial stage of the disease the pathological feature in the light reflex was a disproportion between the primary phase of contraction on the one hand, and the secondary and tertiary phases on the other; the former were preserved and the latter decreased or absent. This disproportion is known to be due to a central sympathetic condition. In all cases of advanced simple glaucoma, and frequently in the initial stages as well, other modifications were detected; the primary phase of contraction was sluggish and less extensive and was preceded by a longer latent period than usual. In cases of unilateral simple glaucoma the clinically unaffected eye showed pupillographic features characteristic of simple glaucoma. In some cases the pupillary disturbances were of purely central sympathetic origin; in others the sympathetic type was modified by ocular factors. The authors consider that the presence of characteristic pupillary disturbances in the clinically unaffected eye suggests the presence of latent glaucoma in that eye. This assumption involves the supposition that demonstrable increased intraocular pressure is preceded by centrally conditioned pupillary disturbances. They point out that intraocular hypertension is only one symptom in a syndrome in which ocular hypertension, lesions of the receptor and effector organs within the eye *et cetera* exist as equivalent expressions of the same central lesion. Each symptom may be more or less developed or even clinically unascertainable. This observation holds for intraocular hypertension as well as for other symptoms. The authors conclude that, although lesions of the central nervous system appear to play an important role in the genesis of simple glaucoma, it is uncertain whether such lesions, although organic, are primary or secondary to other ætiological factors, such as nutritional deficiency and toxicosis.

O. LOWENSTEIN AND M. J. SCHOENBERG (*ibidem*) have studied the pupillary reactions of the seemingly unaffected eye in clinically unilateral simple glaucoma. They state that in all the cases studied, pupillary disturbances accompanied the glaucomatous process through all stages from the earliest. These pupillary disturbances proved to be bilateral, even when the glaucomatous process appeared clinically to be unilateral. Analysis of the pupillographic observations on the clinically unaffected eye shows that a central nervous factor in the genesis of pupillary disturbances is always demonstrable; functional modifications of either the retina or the optic nerve or both are frequently, but not always, present. The authors do not hold that a causal connexion exists between the pupillary disturbances and the glaucomatous process, but they assume that both may be entirely or partially due to the same genetic factor. This assumption explains the constancy with which pupillary disturbances accompany the glaucomatous process. In view of this constant connexion between pupillary disturbances and the glaucomatous process, and of the presence of pupillary disturbances in the clinically unaffected eye, the authors consider that the pupillographic examination appears to promise a new way of establishing a diagnosis of *glaucoma simplex* in the pre-clinical stage.

Primary Carcinoma of the Lachrymal Sac.

W. L. ROBERTS AND J. R. WHEELER (*The British Journal of Ophthalmology*, May, 1944) report a case of primary carcinoma of the lachrymal sac. They point out the rarity of this condition. The patient first noticed watering in the right eye in November, 1942. The condition persisted, and one month later a tender swelling was noticed over the right tear sac; the swelling later became painful. No symptoms referable to the nose and throat were present. The watering persisted, but at no time did the patient complain of purulent discharge from the right eye. He was sent for examination in March, 1943. At that time visual acuity of both eyes was $^6/_6$ with correction. Slight

injection of the palpebral conjunctiva of the right eye was noticed. The media and fundi of both eyes were normal. In the region of the right tear sac there was a firm and slightly tender mass the size and shape of a bean. In April, 1943, the patient noticed blood-stained discharge from the right nasal passage and nasal obstruction in that area. In July he was admitted to hospital, and examination revealed a great increase in the size of the swelling in the right lachrymal sac; the mass was tender to palpation. Surgical removal was undertaken. Pathological examination of material from the lachrymal sac revealed some resemblance to oat-cell carcinoma of the lung; material from the mass in the nose was thought to be relatively malignant, but likely to spread by direct extension rather than by metastasis, and to be moderately radio-sensitive. Radium was implanted. In October, 1943, the patient was in good condition and there was no evidence of recurrence.

Ocular Angiospasm.

S. R. GIFFORD (*Archives of Ophthalmology*, June, 1944), from the records of 23 patients, presents additional evidence that peripheral angiospasm is the cause of what has been described as central angiospastic retinopathy. In a certain proportion of young adults with *periphlebitis retinæ* and recurrent hæmorrhage in the vitreous, peripheral vascular disease is the primary cause. In one case of extreme attenuation of the retinal arterioles with considerable peripheral angiospasm following operation for cataract, antispasmodic treatment produced improvement. In all cases presenting the characteristics of the three syndromes, central angiospastic retinopathy, periphlebitis of the retina and arteriolar spasm of the retina, careful examination of the peripheral vascular system is indicated. In other conditions, when it is thought desirable to employ vasodilators, such an examination should be made before treatment is instituted.

Vasodilators in Fundus Disease.

W. V. STEPHENSON (*American Journal of Ophthalmology*, June, 1944) has investigated the efficacy of vasodilator drugs in the treatment of various acute diseases of the fundus. His clinical material consisted of more than sixty patients, and the conditions from which they were suffering included the following: early and late syphilitic optic atrophy, acute chorio-retinitis (of tuberculous, toxoplasmic and focal origin), acute retrobulbar neuritis, optic neuritis and alcoholic amblyopia. At the end of one year a complete report of the visual acuity, ocular abnormality and results of treatment was prepared. In no case had the slightest improvement occurred. The author concludes that recent enthusiastic reports of the value of vasodilator drugs in fundus disease are unjustified.

OTO-RHINO-LARYNGOLOGY.

Histologic Otosclerosis.

STACY R. GUILD (*Annals of Otology, Rhinology and Laryngology*, June, 1944) reports that in the otological research laboratory of the Johns Hopkins Medical School serial sections of the temporal bones of 1,161 patients were examined for evidence of otosclerosis. Histological evidence of the disease was found in 49 cases. The areas of bony change were found in several places, and in a large number the lesions were multiple. Otosclerosis was present anterior to the oval window in 65 of 81 affected ears, however. Hearing tests, including the preparation of audiograms, were available for 55 of the 81 ears in which histological examination later revealed otosclerotic areas. Without exception the material on which this report is based supports the belief that otosclerosis does not cause an impairment of hearing unless a bony connexion becomes formed between some part of the oval window margin and the stapes foot plate. Several photomicrographs reveal extensive encroachment upon the oval window without ankylosis, yet the hearing had been normal. Cochlear degeneration was not found to be more frequent in the otosclerotic cases than in those in which the bony changes were absent.

Deafness Resulting from Gunfire and Explosions.

STEPHEN SUGGIT (*The Journal of Laryngology and Otology*, August, 1943) has studied 69 injured ears among patients admitted to a Royal Naval hospital. Middle ear deafness, commonly due to rupture of the tympanic membrane, occurred in eighteen cases. Repeated or prolonged exposure to explosive noise was found often to cause a gradual drop in the audiometer curve, the drop often commencing at 512 cycles and increasing in the higher frequencies. Abrupt high tone loss is to be observed in persons exposed to blast injury. In these cases damage appears to be permanent, but not progressive. The author remarks upon the fact that many who are exposed to explosive blast escape damage to their hearing. In practice it is found that ear injuries of all types occur more often from small calibre than from the larger calibre guns.

Injection of the Tympanum for Chronic Conductive Deafness and Tinnitus Aurium: The Use of Ethylmorphine Hydrochloride.

B. C. TROWBRIDGE (*Archives of Otolaryngology*, June, 1944), with the work of Grey in mind, in which thyroxin was injected into the tympanum with the object of producing vascular engorgement, has used ethylmorphine hydrochloride in a similar manner. It is stated that this drug has been successfully employed in ophthalmology in efforts to remove pupillary and corneal opacities. The drug is held to produce a sterile inflammatory reaction with subsequent absorption of scar tissue. Patients suitable for treatment are those with deafness of the chronic conductive type without active infection and with an active inner ear and eighth nerve. Local anæsthesia of the tympanic membrane is induced by the close application of a wick saturated in cocaine 10% in aniline oil. Four minims of a 1·5% solution of ethylmorphine hydrochloride are injected through the tympanic membrane and the patient's head is then inclined backwards for ten minutes to prevent escape of the fluid by way of the Eustachian tube. Subsequently at intervals of four to seven days further injections are given, solutions of 1·5%, 2·5%, 3·0% and 3·5% respectively being used. Supplementary politzerization, Eustachian catheterization and tympanic massage are thought to aid in the breaking down of adhesions. An inflammatory reaction commencing after six hours and lasting up to four days is observed in the tympanic membrane. Occasional transient vertigo has been reported. Pain is rarely present and no untoward effects have been observed. In a series of 22 cases, improvement in hearing occurred in 18, lessening of tinnitus occurred in six, and the symptoms ceased in three. Results were controlled by audiometric studies and by the statements of the patients themselves.

Mucocele in Frontal and Ethmoidal Sinuses.

H. M. GOODYEAR (*Annals of Otology, Rhinology and Laryngology*, June, 1944) states that since the establishment and maintenance of a patent, epithelium-lined passage between the fronto-ethmoidal region and the nasal cavity are so frequently difficult, he avoids exposure and removal of the walls and lining from above. Instead he claims success in many instances by punching away the floor and inner wall of the expanded ethmoid bulla. When necessary adequate space for instrumentation and for subsequent drainage is secured by submucous resection of the nasal septum and partial resection of the frequently expanded middle turbinate bone. After wide intranasal drainage has been provided, it is claimed that the bulging commonly found at the inner canthal region can be simply pressed back into place and that diplopia is thus usually readily overcome. Convalescence is greatly shortened and the after-treatment required is limited to measures to control excessive granulations.

Acute Tonsillitis: Treatment by Rectal Administration of a New Bismuth Compound.

J. S. STOVIN (*Archives of Otolaryngology*, March, 1944) quotes the original publication of Monteiro, of Brazil, and later records of others, advocating the intramuscular injection of a bismuth compound, originally in cases of Vincent's infection of the oral cavity, and later in the treatment of tonsillitis. Evidence of the association of Vincent's organisms with acute an chronic tonsillitis is also mentioned. Without any definite claim being made to the fact, it is implied that this association may be one reason why bismuth is often effective in the treatment of most types of acute tonsillitis. An accumulation of bismuth in the tonsils has been demonstrated eight to twenty-four hours after intramuscular injection. The author now reports successful treatment of acute tonsillitis following the administration of bismuth *per rectum* in the form of suppositories containing 0·135 gramme of the bismuth salt of heptadiencarboxylic acid. This preparation is apparently non-irritating and is readily absorbed from the rectum. Rarely are more than two suppositories required to relieve the symptoms. The author quotes results from a series of forty cases in which this form of treatment has been used.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Queensland Branch of the British Medical Association was held on July 7, 1944, at the Mater Misericordiæ Public Hospital, South Brisbane. The meeting took the form of a series of clinical demonstrations by members of the staffs of the Mater Misericordiæ Public Hospital and the Mater Misericordiæ Children's Hospital. Parts of this report were published in the issues of November 4 and November 18, 1944.

Amputation under Refrigeration Anæsthesia.

DR. J. R. S. LAHZ showed a male patient, aged fifty-five years, who had been admitted to hospital on June 29, 1944, with his left leg almost severed just above the ankle, having been run over by a train. The limb was widely bruised and contused, and numerous cuts were present. The tibia was bare of flesh for six inches above the ankle joint. The patient was suffering from shock; his systolic blood pressure was 100 millimetres of mercury and the diastolic pressure was 60. One-quarter of a grain of morphine was given and 1,000 international units of tetanus antitoxin were administered by hypodermic injection. Two grammes of sulphanilamide were given orally. One hour after his admission to hospital the limb was shaved and washed, and a three inch band of cracked ice was firmly applied circularly around the thigh, five inches below the groin. Half an hour later the ice was removed, the limb was elevated for four minutes and a tourniquet was applied at the site. Morphine (one-eighth of a grain) was administered, and the limb was packed in cracked ice from above the level of the tourniquet to and including the foot. The patient was taken to the operating theatre and the limb was washed with iced water and soap and painted with tincture of iodine. With the tourniquet still in place, the limb was amputated five inches below the knee. No anæsthetic agent was administered, the refrigeration being thoroughly adequate in this respect. The patient chatted during the operation, and winced once only, when the tibial and peroneal nerves were pulled down before section. Ten minute recordings of the blood pressure and pulse rate were made. At the time of the patient's arrival at the operating theatre, the systolic blood pressure was 80 millimetres of mercury and the diastolic pressure was 60; at the conclusion of the operation the systolic blood pressure was 115 millimetres of mercury and the diastolic pressure was 70. The pulse rate was 100 per minute on the patient's arrival at the operating theatre and 96 at the conclusion of the operation.

Dr. Lahz said that the clinical condition seemed to improve during operation. Sensation and motor power in the stump were normal after operation. The stump and flaps were healthy one week later, at the time of the meeting. The patient suffered a moderate blood dyscrasia from the sulphanilamide treatment, which had been continued after operation.

Dr. Lahz's second patient was aged sixty-seven years, and had been admitted to hospital on June 8, 1944, with spreading gangrene of the dorsum of the left foot, of arteriosclerotic origin. There was no arterial pulsation in the foot, and the collateral circulation was extremely poor. Amputation was performed on June 15, a ten-inch high stump being left. Refrigeration anæsthesia was used, with the same technique as outlined earlier, except that in the case under discussion the limb could be prepared thoroughly before the patient was taken to the operating theatre. The discomfort of washing the limb in ice-cold water was avoided. The tourniquet had been in place for three hours before operation. Anæsthesia was perfect, apart from a wince of pain as the nerves were pulled down before section. The blood pressure before operation was 170 millimetres of mercury, systolic, and 95, diastolic, and at the end of the operation 150 millimetres of mercury, systolic, and 90, diastolic. The pulse rate did not rise; it was 90 per minute throughout. As could be seen, the flaps were beautifully healthy, although a long anterior flap had been used to cover the stump. No motor or sensory loss was present in the stump. Convalescence was uneventful.

Dr. Lahz said that Newman, in an article entitled "Shockless Surgery: Ice Anesthesia" (*The Scientific American*, April 4, 1942), had well named this method of anæsthesia. There was a large literature describing the technique. Crossman, Allen *et alii* (*Anesthesia and Analgesia*, September, 1942) stated that "lives have been saved by using cracked ice as the sole means of anæsthesia for amputation". The advantages of the method were: (i) no further anæsthesia was needed; (ii) in traumatic cases, bacterial invasion was prevented by early refrigeration anæsthesia and operation, when amputation was necessary; (iii) no shock was caused by the operation, nor any other systemic disturbance; (iv) the flaps appeared healthier; (v) infection after operation was said to be less; (vi) healing appeared to be more rapid after amputation for "vascular gangrene". There were no contraindications. Special arrangements had to be made to catch the water from the ice, a trough being the most convenient way of avoiding mess. Otherwise the sister in the ward had to be pacified in that regard. In both cases discussed, the comfort and health of the patient during and after operation were pronounced.

Septic Arthritis.

Dr. Lahz finally showed a child, aged nine years, who had been admitted to hospital on May 5, 1944, with purulent *otitis media*. The discharge from the ear ceased on May 8. He complained of pain in the right hip region on May 9; the pain was severe on May 11. Examination revealed acute pyogenic arthritis of the right hip joint. The X-ray films revealed no bony changes. The right hip joint was drained through a Smith-Petersen incision the same day. Copious sero-purulent fluid, loaded with lymph flakes, was evacuated from the joint. The patient was subsequently nursed in extension with the limb abducted and the thigh slightly flexed. Culture of the fluid from the joint yielded *Streptococcus pyogenes*. Relief clinically was immediate, and there was a rapid subsidence of pyrexia. A thin, purulent discharge was still present by the eighteenth day, varying in amount from day to day, and resistant to sulphadiazine therapy. X-ray examination of the joint on that date still revealed no bony changes. The administration of penicillin extract was then commenced intramuscularly in the right thigh, 20,000 units being given every one and a half hours, till 1,500,000 units had been administered over a period of four and a half days. The discharge had ceased by May 28, ten days after penicillin administration was begun. At the time of the meeting the wound was completely healed and there was a full and painless range of movement in the hip joint. The patient was afebrile and was in good, bounding health. The limb had been released from extension two weeks before. An X-ray examination made two days previously revealed pathological changes in the neck of the femur; a rather large area of rarefaction of a patchy nature, well defined by a peripheral ring of slight condensation of bone, was present on the inferior aspect of the neck of the femur, adjacent to the epiphysis.

Dr. Lahz said that it was clear that the condition was a pyogenic infection of the right hip joint, concomitant with and due to osteomyelitis of the neck of the femur. It was too early to say whether the cure was permanent. The well-being of the patient, however, and the normal state of the hip joint and surrounding tissues, would point to cure. The result was in contrast to those previously experienced in osteomyelitis of the neck of the femur. Such a result gave one a hope that, in osteomyelitis of the neck of the femur with infection of the joint, chemotherapeutic treatment with early evacuation of the joint would lead to better results than those previously achieved. Referring to the administration of penicillin, Dr. Lahz said that they had been giving it in their small series intramuscularly, and they found the objection of the patient to frequent intramuscular injection extreme. Therefore, they now, with full aseptic technique, inserted a long small-bore needle into the *vastus lateralis*; the penicillin was injected slowly. The needle was then withdrawn half an inch. The hub of the needle rested on a sterile pad. At the end of the injection, the nurse covered the area with a disinfectant pad. When she gave the next injection, she pushed the needle in half an inch, gave the injection, and again covered the area with the disinfectant pad. The needle and the site were changed every twenty-four hours. Children had no objection to this method, and no penicillin was lost.

(To be continued.)

Correspondence.

MUSCLE AS A HÆMOSTATIC.

SIR: The writer of your "Current Comment" (1944, Volume I, page 516), referring to the arrest of hæmorrhage during

the course of operations on the brain, remarks: "The application of muscle, as practised by Cushing, is effective." This is so strikingly effective that it always appears somewhat miraculous to me, especially when a small piece of muscle gently held for a few moments on a torn venous sinus from which a lake of blood has been welling arrests the flow as if by magic.

Although no one for one moment would dispute the great debt that modern neurosurgical practice owes to Harvey Cushing, we would, however, do well to remember that this use of muscle was introduced by Victor Horsley. In Harvey Cushing's reference to it in his paper on hæmostasis which appeared in 1911 (*Annals of Surgery*, 1911, Volume LIV, page 1) he pays Horsley due credit for priority, remarking in a footnote that since his (Cushing's) paper was put together he had learned from "Dr. Lund's interesting report of the visit last summer of the Society of Clinical Surgery to Great Britain that Sir Victor Horsley demonstrated the hæmostatic action of a fragment of muscle on the exposed brain".

Horsley apparently did not record his observations until three years later. In a "Note on Hæmostasis by Application of Living Tissue" (*British Medical Journal*, 1914, Volume II, page 8) he credits "the late Dr. Wooldridge" with stimulating his idea that "probably the best material would be living vascular tissue—that from the (injured) surface of a cut fragment of muscle". Horsley investigated the problem in detail and found that by direct experiment on the divided arteries of animals, muscle hæmostasis would resist blood pressures of as much as 60 to 80 millimetres of mercury and that boiling lessened the effectiveness of the muscle. He also studied microscopically the changes which took place at the site of application of the muscle fragments.

The late T. de Martel, of Paris, developed the procedure further by using fresh avian muscle which he believed to be particularly rich in thrombogenic elements. Pigeons were kept at his clinic, killed as required, and pieces of fresh pectoral muscle brought into the theatre to effect the hæmostasis. Those of us who have seen this carried out in Dr. de Martel's clinic, which it was always such a pleasure to visit in the days before the war, must feel sad just at this time, when Paris has been freed from the invader, to recall his death on the day the Germans entered the city.

It is often difficult to ascribe credit for priority correctly, but it would appear that Victor Horsley, a true pioneer of neurosurgery, should be credited with the introduction of muscle as a hæmostatic.

Yours, etc.,

LAMBERT ROGERS,
Surgeon Captain, Royal Naval Volunteer Reserve.

C.o. Admiralty,
London, S.W.1,
September 7, 1944.

NOTE ON CUTANEOUS LEISHMANIASIS IN THE TERRITORY OF PAPUA.

SIR: Dr. A. J. May, in his "Note on Cutaneous Leishmaniasis in the Territory of Papua", published in THE MEDICAL JOURNAL OF AUSTRALIA, November 4, 1944, states that I confirmed the presence of Leishman-Donovan bodies in smears from his cases.

This statement is incorrect. In some smears which were examined at the request of Mr. Christian, I saw intracellular organisms resembling the Donovan bodies commonly found in smears from cases of *granuloma inguinale*. I saw nothing resembling the Leishman-Donovan bodies, which are characteristic of cutaneous leishmaniasis.

Cutaneous leishmaniasis has never, to my knowledge, been observed in Papua or the neighbouring islands.

Yours, etc.,

A. V. JACKSON,
Major, Australian Army Medical Corps.

November 14, 1944.

TRAUMATIC MONOCULAR GLAUCOMA.

SIR: In THE MEDICAL JOURNAL OF AUSTRALIA of July 29, 1944, there appeared an article on traumatism as a cause of chronic glaucoma. While complimenting Dr. D'Ombrain on his original observations on this previously unknown cause of a serious eye disease, I desire to add one recent case of my own to the five cases recorded by him.

Mr. K., aged forty years, in June, 1944, gave a history of loss of vision in the left eye of gradual onset. Visual acuity was $^{6}/_{6}$ in the right eye and $^{6}/_{60}$ in the left eye. There was marked cupping of the left disk. Tension in the left eye was sixty millimetres of mercury. The right eye was normal in every respect. *Guttæ Pilocarpinæ* were prescribed and he was asked to return in August.

Meantime I had seen Dr. D'Ombrain's paper, so when the patient returned I questioned him and elicited the following history. In 1931 he had been struck on the left eye by a piece of wood. Slight concussion of the brain and traumatic mydriasis followed. He was in hospital for a week and subsequently attended an eye hospital for some weeks. In August, 1944, vision in the left eye was $^{6}/_{60}$; cupping was as before and the tension was high. I therefore did an Elliot trephining operation using a 1·5 millimetre trephine. Recovery was uneventful and he returned home. The right eye was normal in all respects. I think it will probably be found that these traumatic monocular glaucomas are not uncommon.

Yours, etc.,

J. C. DOUGLAS, L.R.C.P. and S. (Edinburgh), D.O. (Oxon.),
Honorary Ophthalmic Surgeon, Ballarat Hospital.

Ballarat,
Victoria.

SCRUB TYPHUS.

SIR: In connexion with the outstanding article on scrub typhus published in the issue of November 18, 1944, may I as a consultant and repatriation doctor who sees some of these men bring out two points which Lieutenant-Colonel Williams *et alii* have not emphasized, probably because he did not realize their importance.

1. The heart manifestations. As Colonel Williams points out, there are those of a toxic myocardial change which is effective during the acute stage—but leaves no permanent damage. There is a belief held, I am sorry to say, by both medical men and soldiers that during or even after convalescence extra exertion may cause sudden and fatal heart failure. The emotional effect of this view may be imagined—we had "D.A.H." after influenza and trench fever; it will be nothing to the "D.A.H." we shall have after typhus.

2. The paralyses of limbs, which are not uncommon, equally seem to clear up completely. But they may be very possibly continued as purely hysterical conditions. Such a case was seen recently at Rosemount Repatriation Hospital where a quadriplegia and partial anæsthesia seemed permanent. Electrical testing, however, showed a normal reaction in all muscles and he left the hospital walking freely. The moral is that all such cases should be tested by faradic current after a few weeks if the paralysis seems to persist.

These are small points which do not come into the problem as Lieutenant-Colonel Williams has seen it—and which he has so excellently described.

Yours, etc.,

S. F. MCDONALD.

217, Wickham Terrace,
Brisbane.

Obituary.

JOHN FULLARTON MACKEDDIE.

WE are indebted to Dr. John Kennedy for the following appreciation of the late Dr. John Fullarton Mackeddie.

John Fullarton Mackeddie was born on June 30, 1868, in a humble highland home at Fortrose (near Inverness). He won a scholarship at the local academy, which took him to Edinburgh University. After taking his B.A. degree, he taught Greek and Latin until he came to Australia in the late 'eighties. Apparently undecided as to a career, he filled the interim in teaching appointments, and was a theological student at Ormond College for a time. He was house master at Geelong College from 1893 to 1896, and with Mr. Buntine at Caulfield Grammar School from 1896 until 1901, when he graduated in medicine. It is interesting to note that quite

a number of "his boys" of these years afterwards became well known in the medical world, Caulfield Grammar School alone having no less than ten specialists.

During his medical course he gained honours every year; shared the exhibition in anatomy in his second year and won it in his third year.

He joined Dr. McPhee and Dr. Major as resident medical officer at the Alfred Hospital in 1902, where he remained for two and a half years. He obtained the degree of Doctor of Medicine in 1904; resigned from the Alfred Hospital and began practice as a physician in Collins Street. He was appointed clinical pathologist to the Alfred Hospital in that year and pathologist to the Metropolitan Asylums in 1905. He was acting out-patient physician at the Melbourne Hospital during the late Sir Richard Stawell's absence abroad in 1907.

At the retirement of the late Dr. Jamieson in 1909, he was appointed physician to in-patients at the Alfred Hospital and lecturer in medicine; dean of the clinical school in 1928 and consulting physician on his retirement in 1933.

As a resident, Mac's energy, force of character and personality made itself felt in the hospital. Older than most resident medical officers, with some years of experience behind him, he was not over-awed by custom or a conservative Board of Management. A laboratory was wanted; he created one, commandeering an unused ward to do so. The medical wards were kept light during the off typhoid period; he filled them with sick people and kept them thus all the year; was even known to dispense with a bath for the very ill patient in that dignified conservative old place. There is no doubt that he was encouraged and helped in this work of rejuvenating by the late Dr. A. V. M. Anderson and the appointment of Mr. Hamilton Russell and Mr. James Buchanan to the staff. It was this work and the rapid progress he made as consulting physician which determined his appointment as in-patient physician in 1909 without serving in the out-patient department.

The clinical school was established in 1910, and he once again became a teacher. For this his years of work had trained him; he had learned the hard way of getting knowledge into brains. It was not sufficient to talk a subject at the bedside; every clinic was not only a lucid, dogmatic exposition, but as far as possible a practical demonstration, void of padding with the main essentials standing out, leaving the minor details to take care of themselves. Few of the old students will forget these clinics or the kindly teacher who opened up his home for them at Frankston for the working holidays. Thus, as a clinical teacher it can be said that he established a tradition which will last as long as there is a school at "the Alfred".

As a physician he was probably at his best in disease of respiratory and nervous systems, although he devoted considerable attention to other parts of general medicine, and for some years he kept a small hospital filled with chronic joint cases. He was a "keen observer", had fine clinical sense, and had been taught to use his eyes, ears and hands by men of the old school like the late John Williams.

His great sympathy, patience, human kindness and dominating personality easily obtained the confidence of any patient. He was a born psychologist and made full use of this in treating the diseased body as well as the disordered brain. As a diagnostitian the words of a colleague come to mind: "When Mac has finished there is nothing left for anyone else to find."

He went abroad in 1923, and for two years became a student again. The late Mr. Tom Baker was in England with him, and on his behalf he investigated the value of Spahlinger's treatment of tuberculosis. There is no doubt that had the claim made for this been supported by results, it would have been acquired for Australia.

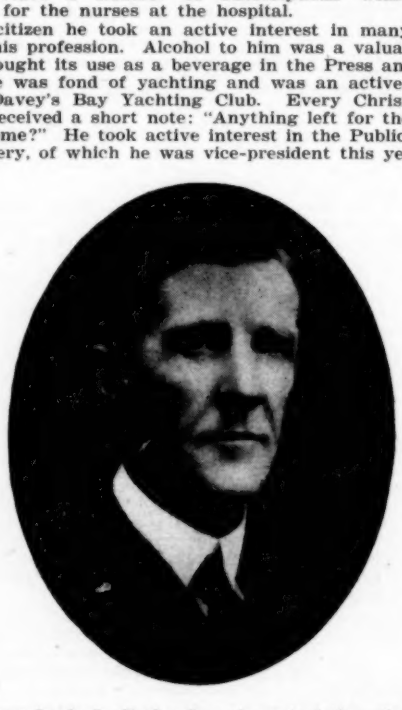
The idea of a research laboratory at the Alfred Hospital developed out of this visit to England and resulted in the establishment of the Baker Institute, with the late Dr. Penfold as its first director and Dr. Mackeddie as chairman of the Trust. From then on he devoted half his working time to the hospital, applying the knowledge he had acquired abroad, that is, the value of cisternopuncture, encephalography, the use of lipiodol in the diagnosis of cerebro-spinal and lung diseases, as well as the value of lung collapse in tuberculosis. Following this came special clinics in asthma and diabetes, and attempts to combine the Baker research activities with the investigation of patients in the wards. No one but a man gifted with his personality, drive and energy could have carried the burden. Never for one single day was the patient or the student neglected. From this work grew the neurological, the diabetic and asthma clinics at the hospital.

In 1924 he presented his work on lipiodol and lung conditions to the congress at Auckland, and in 1931 to the British Medical Association in Melbourne.

No record of his hospital work can be complete without reference to his interest in the training and welfare of the nurse. For many years, even though he was probably the busiest physician in Melbourne, he found time to give his nursing lectures and to see that the principles he taught were carried out in the wards. For over forty years he organized and conducted the Christmas carol singing; he hired the pianos and brought artists for the solo singing.

Fond of reading himself, he encouraged this in others and provided a number of subscriptions with lending libraries for the nurses at the hospital.

As a citizen he took an active interest in many objects outside his profession. Alcohol to him was a valuable drug, but he fought its use as a beverage in the Press and lecture hall. He was fond of yachting and was an active member of the Davey's Bay Yachting Club. Every Christmas his friends received a short note: "Anything left for the Minton Boys' Home?" He took active interest in the Public Library and Gallery, of which he was vice-president this year.



As a man he had all the fine characteristics of the race from which he came and a few of its faults. The worst of the latter was perhaps an inherent highland pride. There was no feudal system in the clan. Probably this made him at times intolerant of opposition, but even that had its blind side.

To his friends he was loyal to the last degree, and a great fighter to have on one's own side. He had no idea of business or of the financial side of his practice, and no fees would have been collected at all had it not been for the pressure of his nurse and household bills. The late Dr. A. V. M. Anderson once remarked to me that if we had all the fees he had not collected we could rebuild the Alfred.

Such was the man we have been privileged to have known and to have worked with, to have loved and to have called friend and colleague. He has left a tradition of sympathy, of kindness, of loyalty, of work for the work's sake—that the patient always comes first, and that because of that the doctor and the nurse must always dominate the hospital.

DR. THOMAS CHERRY writes: Mackeddie in the course of forty-three years of medical practice reached an almost unique position in the ranks of his profession. He was closely identified with the Alfred Hospital during the whole of this period as resident, honorary and consultant, and in particular he established the Baker Institute as an integral part of the hospital. By his selection of Penfold as director and his support of Willis as pathologist, that institute has already placed to its credit two first-class names among Australian scientists. Outside his medical career he became vice-president of the trustees of the Melbourne Public Library with its associated galleries and museums, while a different facet in his character is reflected by the long list of in-memoriam notices inserted in the newspapers by grate-

ful patients, who regarded him as a trusted adviser as well as a wise and friendly family doctor.

The conditions which reinforced his character and helped him to accomplish so much in the course of a very busy life are worth placing on record, for Mackeddie was one of the small minority of medical men who are able to discriminate the comparative importance of things outside their own professional field. He took the degree of B.A. in 1892, and after several years' experience as a teacher in the public schools graduated in medicine in 1901.

A degree in arts as a preliminary to medicine was not infrequently taken in the early years of the university. This was a comparatively simple matter, because Greek and Latin were compulsory, not only for matriculation, but also for first year medicine up to 1876 when natural philosophy became an alternative. Further, chemistry and botany in the first year and comparative anatomy and zoology in the second were subjects common to both arts and medicine. We can therefore understand that a double degree would appeal to many students and tend to give them more than a purely medical standing when in contact with educated men in the community. Nearly ninety years ago, when the opening of a medical school was mooted, the university council seems to have steadily favoured a five-year course probably for two reasons: it gave the student a broader outlook, and it would help to provide larger classes for the four original professors. When Halford arrived as the first medical professor in 1862 he at once made anatomy the central subject in the second, third and fourth years, and in this way he secured for our men a special standing when they went to London and other centres for post-graduate work.

At Ormond College Mackeddie was fortunate in coming under the influence of MacFarland, and also in doing his arts course in touch with a band of enthusiasts. In addition to the veteran McCoy there were Tucker, Laurie, Masson, Spencer and Lyle, and when he returned to his medical course a generation of young men had taken charge of both the scientific and clinical work. Among these there were Allen in anatomy and pathology, Martin and Barrett in physiology, Fitzgerald, Ryan, Syme and Moore in surgery, and Williams, Grant, Stawell and Wilkinson in medicine. Similar advances had been made at the Alfred where the staff included Anderson, Hamilton Russell and Maudsley. The fact that thirteen of these teachers received the honour of knighthood is sufficient testimony to their position in the university and hospital staffs. In the three years 1900, 1901 and 1902 there were 91 medical graduates, and among these I think it may be safely claimed that Mackeddie carved out a special niche for himself.

DR. R. A. WILLIS writes: Of the late Dr. J. F. Mackeddie's work as a physician and as a leader in public affairs, others will write. I wish only to record the gratitude due to his memory by the students of medicine who passed through his hands at the Alfred Hospital; I was one of these in 1919-1921. He was a superb teacher, and he deliberately made the education of his students one of his main activities. His bedside clinics captured and held our interest from start to finish; he taught vividly how to examine a patient, how to elicit physical signs, and how to write histories; and, more than this, he taught us something of his own tact and sympathy in handling and talking to our patients. He gave us a systematic course of tutorial lectures in medicine, accompanied by typescript notes which we treasured for their completeness and clarity. I know that I speak for many others of the students of that period when I say that we will always remember with gratitude "Mack's" clinics and lectures.

DR. A. B. CORKILL writes: As a teacher of clinical medicine Dr. J. F. Mackeddie was unsurpassed. His teaching, although at times unorthodox, was always vivid and stimulating. Further, he had the happy knack of hanging facts together in a way that facilitated their retention. My earliest recollections of Dr. Mackeddie were associated with the clinical school of the Alfred Hospital when as a member of a group of students I was entering fourth year. We had completed some preliminary training at the out-patient department and had been transferred to in-patients. We were awaiting Dr. Mackeddie's arrival in one of the medical wards; this was dramatic, and the forceful personality of the man was immediately apparent. The whole ward seemed to brighten up, and after greetings had been exchanged with patients, the doctor turned his attention to us. Following a short talk on our duties in the ward and particularly those to the patient, we were subjected to a short cross-examination on the auscultation of the heart and lungs. We were very proud of our newly acquired knowledge and quite confident of ourselves. Dr. Mackeddie suggested that we examine a patient on the balcony, said to have a large cavity in his lung. We carried out our examinations and described the sounds that we heard; these covered practically all the text-book descriptions. After solemnly hearing us out Dr. Mackeddie said: "Well, boys, you have been listening to a perfectly normal chest; now go and listen to it again." This was but one example of his teaching methods, but one never forgot facts learned in such a way.

The doctor could take a neurological case and pin facts together in such a way that one could learn an enormous amount of neurology from a single patient.

The patients worshipped Dr. Mackeddie. It was a common occurrence for someone on the balcony, anticipating Dr. Mackeddie's arrival, to play some of Harry Lauder's records on a portable gramophone. Dr. Mackeddie never ignored these gestures and always had a word for the patient before getting on with the work of the ward.

Apart from clinical demonstrations, Dr. Mackeddie used to give a series of lectures on medicine. At the time none of us appreciated the enormous amount of work put into those lectures. In later years I realized that, returning to Frankston after a hard day's work, he would often sit up into the small hours preparing material for his "boys".

From the outset Dr. Mackeddie had always appreciated the importance of a hospital laboratory service, and in his days as a resident he actually set up a small laboratory. At the time this was rather a feat, as there was very little teaching of clinical pathology and biochemistry; in fact the latter hardly existed. In 1923, whilst in London, Dr. Mackeddie was greatly impressed by the clinical biochemistry that was being carried out by Dr. McLean at Saint Thomas's Hospital. At this time there was a boom in laboratory investigations and Dr. Mackeddie determined that the Alfred Hospital should obtain the advantages of these methods. Accordingly he sent for me to come to London and be trained under McLean. I had always learned to expect the unusual from Dr. Mackeddie, but his amazing activities in London came as a complete surprise. A holiday tour with just a little medical work had developed into a strenuous post-graduate course composed of a most heterogeneous set of subjects. The following may give some idea of his activities. Two mornings a week were spent at Brompton Hospital in studying the technique of artificial pneumothorax, then the remaining portion of the week with Dr. McLean at Saint Thomas's Hospital. Here he went back to the bench and learnt the methods of carrying out blood urea, blood sugar, basal metabolism and other similar investigations. To the above list others were rapidly added, such as *cisterna magna* puncture and lipiodol diagnosis. Then there were intensive studies in clinical electrocardiography and chemical examination of the cerebro-spinal fluid. At the time Dr. Mackeddie was in his middle fifties, but he set a pace that many a younger man might have envied.

In London he and his family boarded at Lancaster Gate. Following a day's hard work Dr. Mackeddie would retire to his attic study to review and write up his notes. There he had quietness, the only disturbing factor being a somewhat noisy cistern in a convenience opposite. However, with usual ingenuity this was remedied by placing an "out of order" sign on the door.

On his return to the Alfred Hospital Dr. Mackeddie instructed students and others in the value of biochemical investigations. He initiated the treatment of lung tuberculosis by artificial pneumothorax and the diagnosis of spinal cord tumours by lipiodol. Finally it was owing to his representations that the Thomas Baker, Alice Baker and Eleanor Shaw Medical Research Institute was founded.

Dr. Mackeddie was never happier than when teaching students or planning new things for the Alfred Hospital.

Naval, Military and Air Force.

CASUALTIES.

ACCORDING to the casualty list received on November 23, 1944, Captain M. J. McNamara, A.A.M.C., Mosman, who was previously reported to be a prisoner of war, is now reported missing, believed deceased.

According to the casualty list received on November 25, 1944, Colonel M. G. Loadsman, A.A.M.C., Lismore, has been removed from the "dangerously ill" list.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

THE undermentioned have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1939, of New South Wales, as duly qualified medical practitioners:

Segal, Zara, M.B., B.S., 1944 (Univ. Sydney), Perth General Hospital, Perth, Western Australia.

Sheehy, John Edward, M.B., 1944 (Univ. Sydney), Mater Misericordiæ Hospital, North Sydney.

Snape, Margaret, M.B., B.S., 1944 (Univ. Sydney), St. George District Hospital, Kogarah.

Stanley, Malcolm Roberts, M.B., B.S., 1944 (Univ. Sydney), Sydney Hospital, Sydney.

Starr, Diana Miriam, M.B., 1944 (Univ. Sydney), Royal Hobart Hospital, Hobart, Tasmania.

Starr, Frank John Mitchell, M.B., 1944 (Univ. Sydney), Royal Hobart Hospital, Hobart, Tasmania.

Steinbeck, Alfred William, M.B., B.S., 1944 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Hakendorf, Andrew John, M.B., B.S., 1929 (Univ. Adelaide), Kurraghein Avenue, Elizabeth Bay.

Swaney, Theresa Marie, M.B., B.S., 1943 (Univ. Melbourne), 13, Hunter Street, Singleton.

Change of Name in Register.

Rosenfeld, Israel, 212, Victoria Road, Bellevue Hill; name now Rosenfield, Frederick.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Stuart, Mary Grace, M.B., B.S., 1944 (Univ. Sydney), 90, Bellevue Road, Bellevue Hill.

Lewis, Louis Leonard, M.B., B.S., 1944 (Univ. Sydney), St. George District Hospital, Kogarah.

Alder, Ronald Milton, M.B., B.S., 1939 (Univ. Sydney), 1, Rose Bay Avenue, Bellevue Hill.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Ardill-Brice, Katie, M.B., Ch.M., 1913 (Univ. Sydney), 215, Macquarie Street, Sydney.

Armytage, Jean Edelsten, M.B., B.S., 1935 (Univ. Sydney), 32A, Rawson Street, Epping.

Bennett, Victor Jack, M.B., B.S., 1943 (Univ. Sydney), P.O. Box 17, Millthorpe.

Bird, Eric Lloyd, M.B., 1942 (Univ. Sydney), Flight Lieutenant E. L. Bird, 82, St. George's Crescent, Drummoyne.

Dowd, Bryan Thomas, M.B., B.S., 1943 (Univ. Sydney), Flight Lieutenant B. T. Dowd, R.A.A.F. Station, Tocumwal.

Dowling, John Maxwell, M.B., B.S., 1943 (Univ. Sydney), Mater Misericordiæ Hospital, Crows Nest.

Eakin, Reay Ignatius, M.B., B.S., 1940 (Univ. Sydney), NX203192, Captain R. I. Eakin, 55, Dalhousie Street, Haberfield.

Books Received.

"Vital Statistics and Public Health Work in the Tropics", by P. Granville Edge, with a foreword by Major Greenwood, D.Sc., F.R.C.P., F.R.S.; 1944. London: Baillière, Tindall and Cox. 8½" × 5½", pp. 200. Price: 12s. 6d.

"Varicose Veins, Hæmorrhoids and other Conditions: Their Treatment by Injection", by R. Rowden Foote, M.R.C.S., L.R.C.P., D.R.C.O.G.; 1944. London: H. K. Lewis and Co. Ltd. 8½" × 5½", pp. 136, with many illustrations, some of which are in colour. Price: 12s. 6d.

"The Pathogenesis of Tuberculosis", by Arnold R. Rich, M.D.; 1944. Springfield: Charles C. Thomas. 10" × 6½", pp. 1032, with illustrations. Price: $10.50, post paid.

"Blueprint for the Health of a Nation", by Sir Raphael Cilento, Kt., M.D., B.S. (Adelaide), D.T.M. and H. (England), F.R.San.I. (London); 1944. 8½" × 5½", pp. 196, with illustrations.

"Anatomy and Physiology for Students of Physiotherapy, Occupational Therapy and Gymnastics", by C. F. V. Smout, M.D., M.R.C.S., L.R.C.P., and R. J. S. McDowall, M.D., D.Sc.; 1944. London: Edward Arnold and Company. 9" × 6", pp. 425, with many illustrations. Price: 30s. net.

Diary for the Month.

DEC. 5.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
DEC. 5.—New South Wales Branch, B.M.A.: Organization and Science Committee.
DEC. 6.—Western Australian Branch, B.M.A.: Council Meeting.
DEC. 6.—Victorian Branch, B.M.A.: Branch Meeting.
DEC. 6.—Victorian Branch, B.M.A.: Council Meeting.
DEC. 7.—South Australian Branch, B.M.A.: Council Meeting.
DEC. 7.—New South Wales Branch, B.M.A.: Special Groups Committee.
DEC. 11.—Victorian Branch, B.M.A.: Executive Meeting.
DEC. 12.—Tasmanian Branch, B.M.A.: Branch Meeting.
DEC. 12.—New South Wales Branch, B.M.A.: Medical Politics Committee.
DEC. 13.—Victorian Branch, B.M.A.: Council Meeting.
DEC. 14.—New South Wales Branch, B.M.A.: Branch Meeting.
DEC. 15.—Queensland Branch, B.M.A.: Council Meeting.
DEC. 15.—Queensland Branch, B.M.A.: Annual Meeting.
DEC. 19.—New South Wales Branch, B.M.A.: Ethics Committee.
DEC. 21.—South Australian Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such a notification is received within one month.

SUBSCRIPTION RATES—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rates are £2 for Australia and £2 5s. abroad *per annum* payable in advance.